

FIG. 1

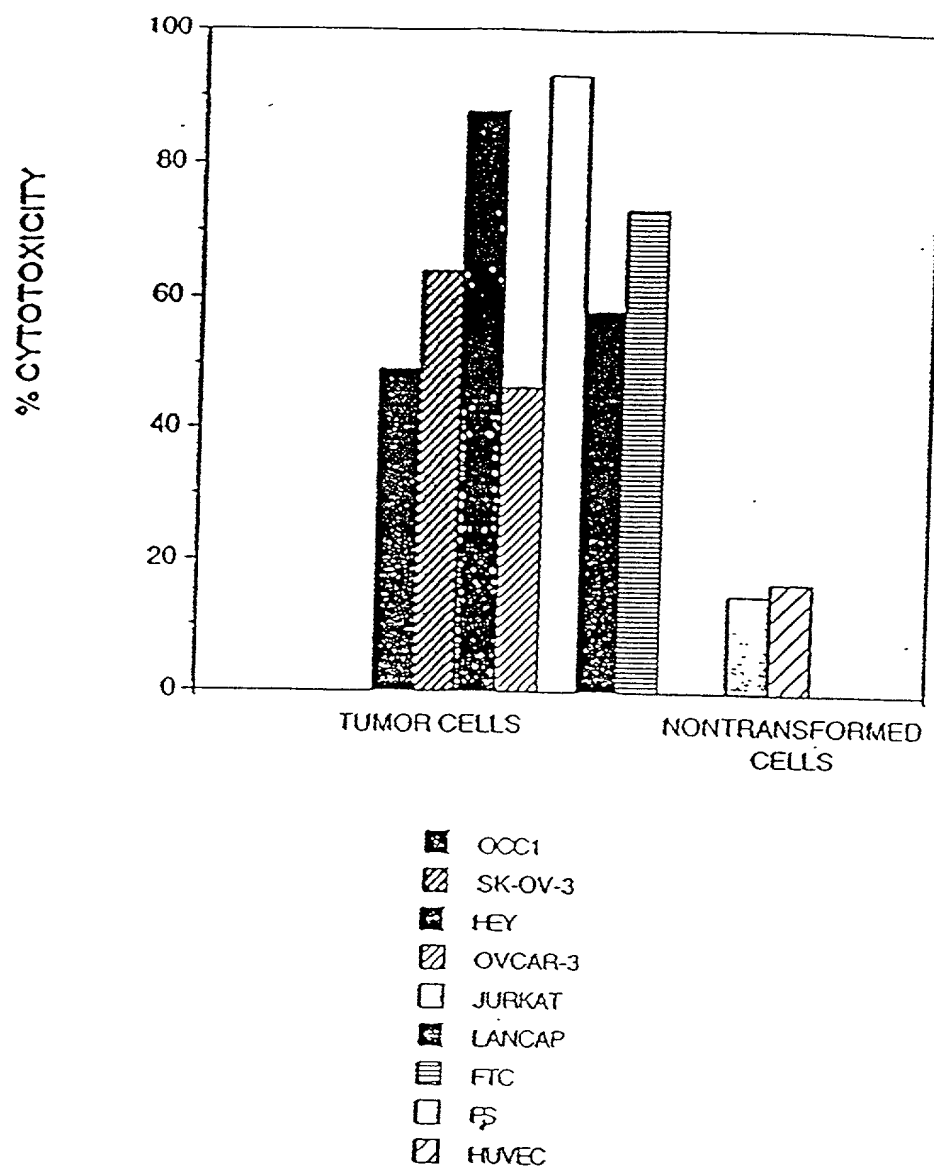
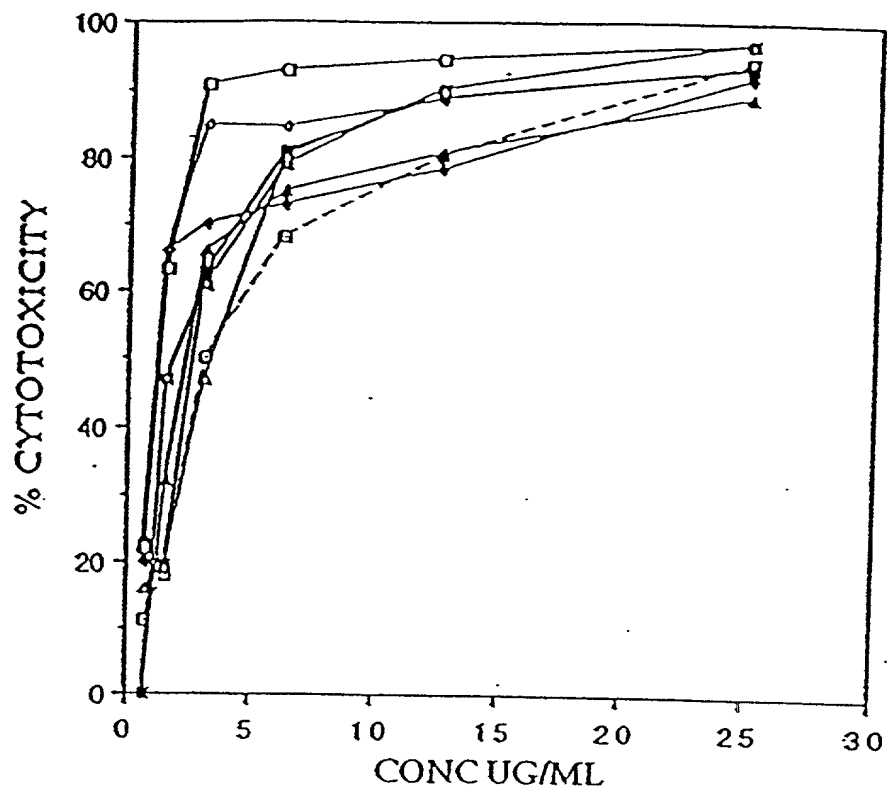


FIG. 2



---□--- HEY
 —●— OVCAR-3
 —□— C-1
 —○— SKOV-3
 —▲— PANC-1
 —□— 769-P
 —▲— 786-O
 —△— A498

FIG. 3

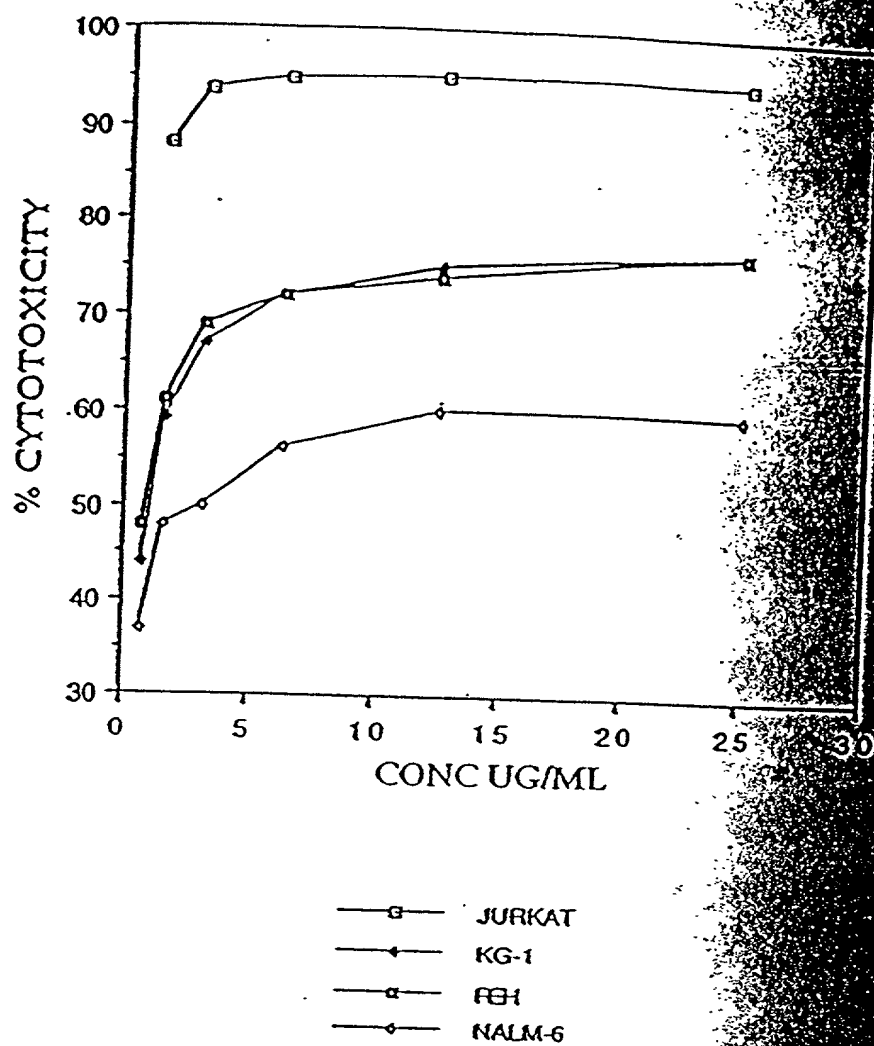
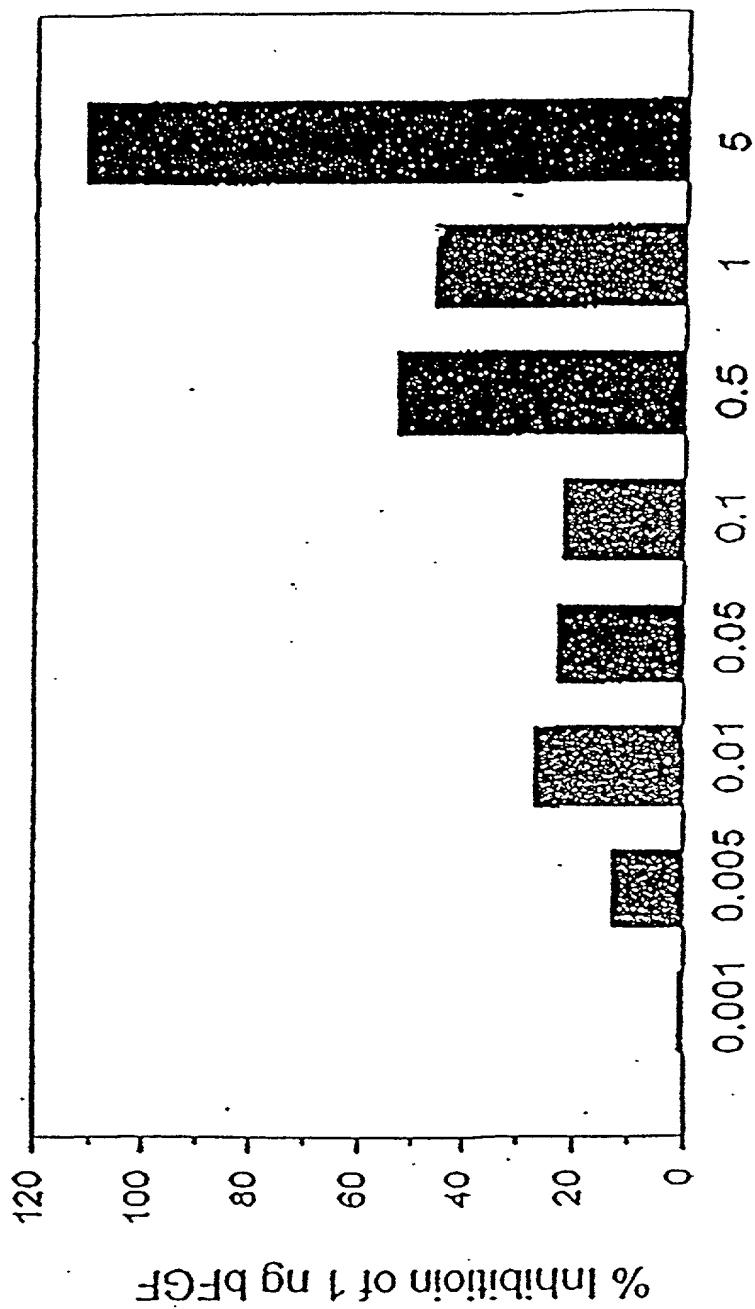


FIG. 4



UA-BRF-004-DELEP F035 $\mu\text{g/ml}$

FIG. 5

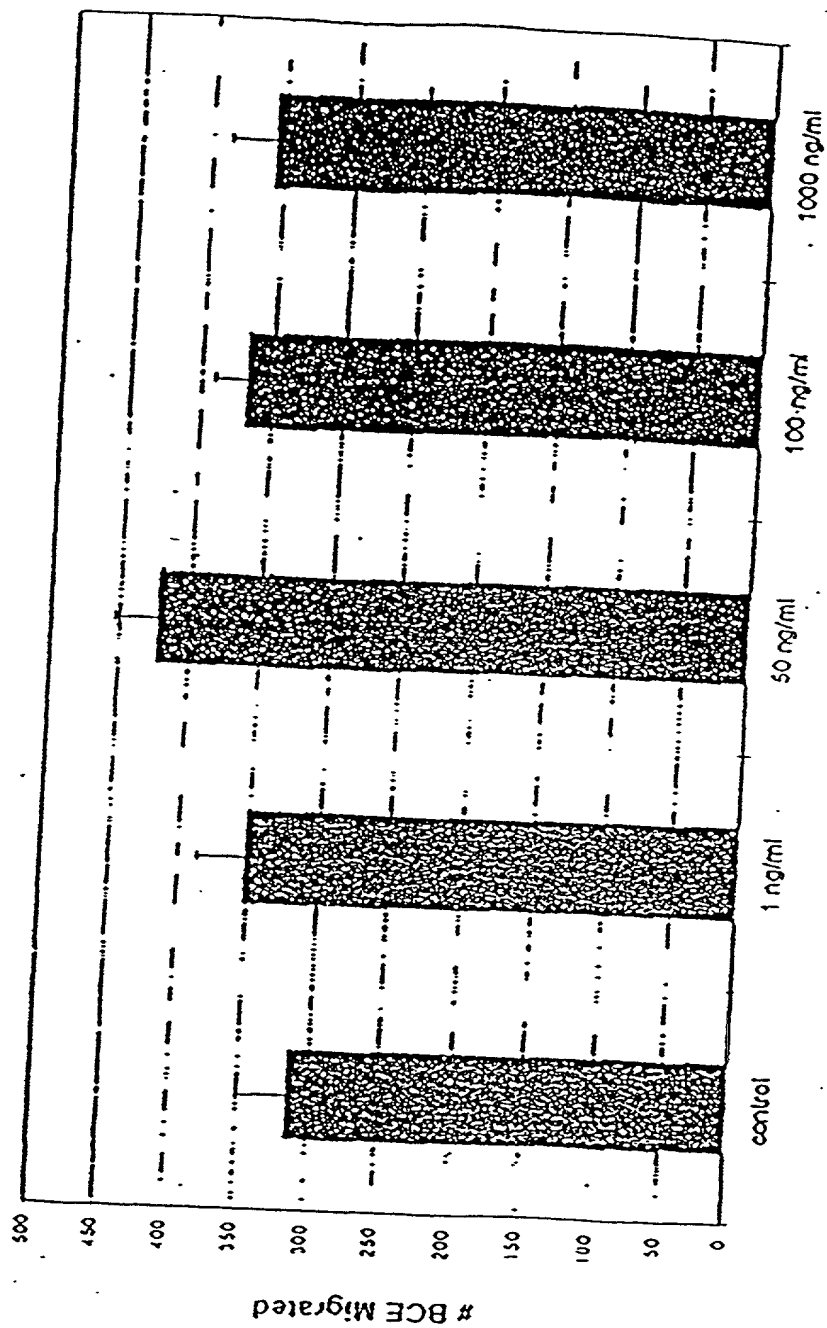


FIG. 6

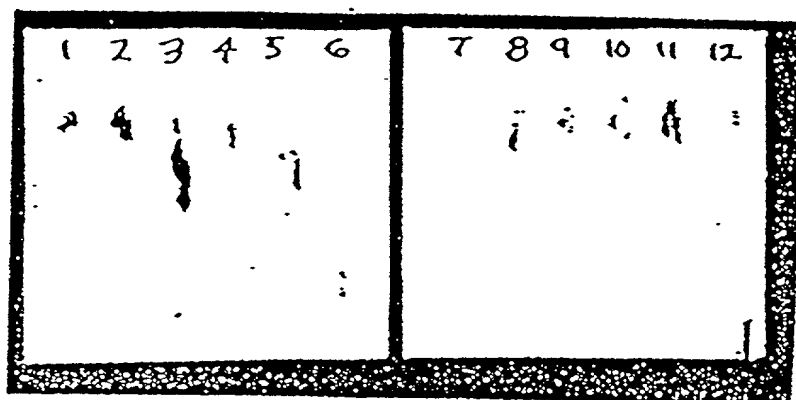


FIG. 7



FIG. 8

Mouse # 133

FIG. 9A

Mouse # 150

FIG. 9B

Dose: 100 nmol

DMBA
4 Weeks

FIG. 9C



Dose: 100 nmol

DMBA
8 Weeks

Mouse # 149

FIG. 9D



Dose: 0.3 mg

Compound # 35
4 weeks

Mouse # 136

FIG. 9E



Dose: 0.3 mg

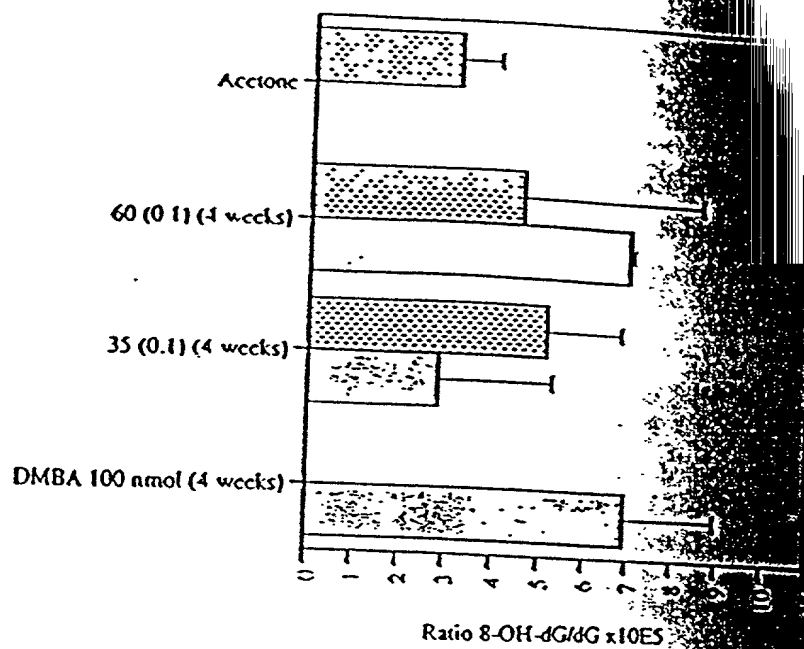
Compound # 35 + DMBA
8 Weeks

Mouse # 140

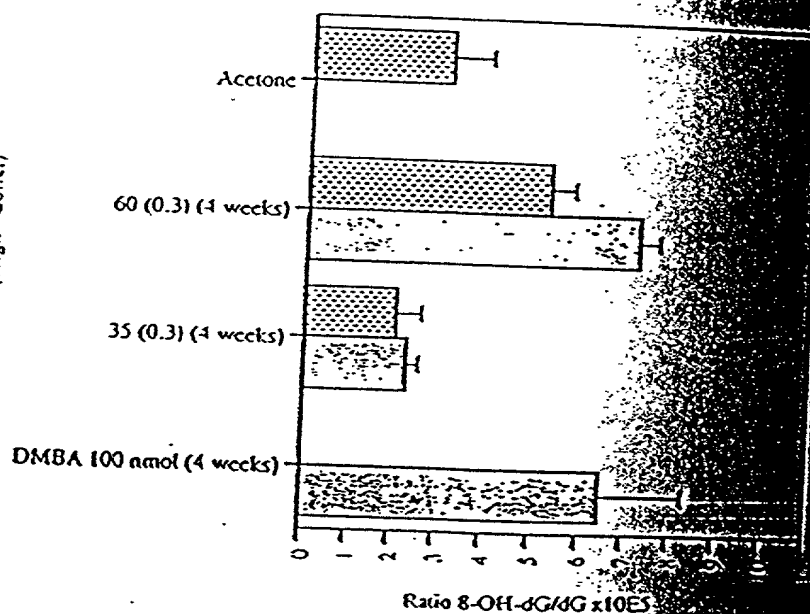
FIG. 9F



Treatment (Low Conc.)



Treatment (High Conc.)





 -DMBA
 +DMBA

FIGURE 10

FIGURE 11

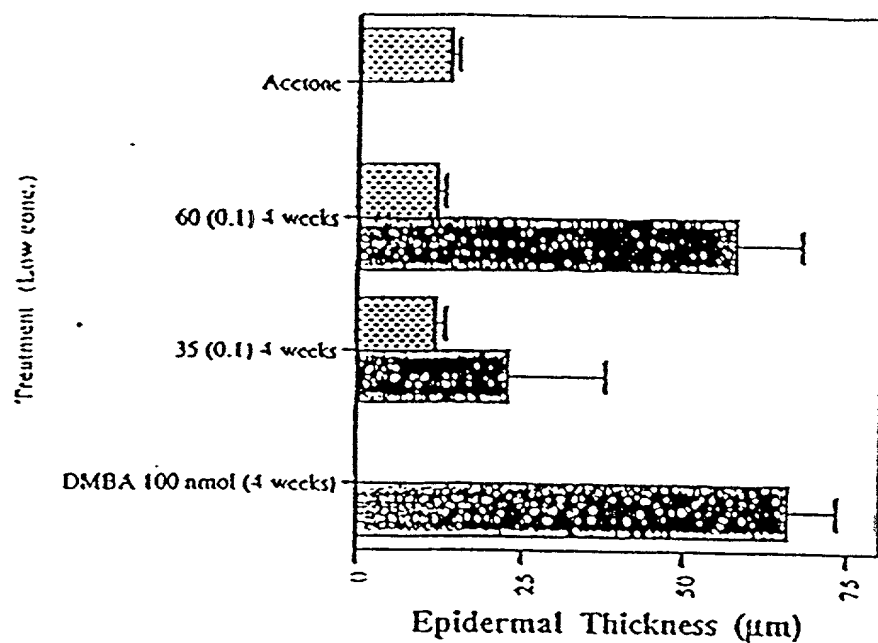


FIG. 11A

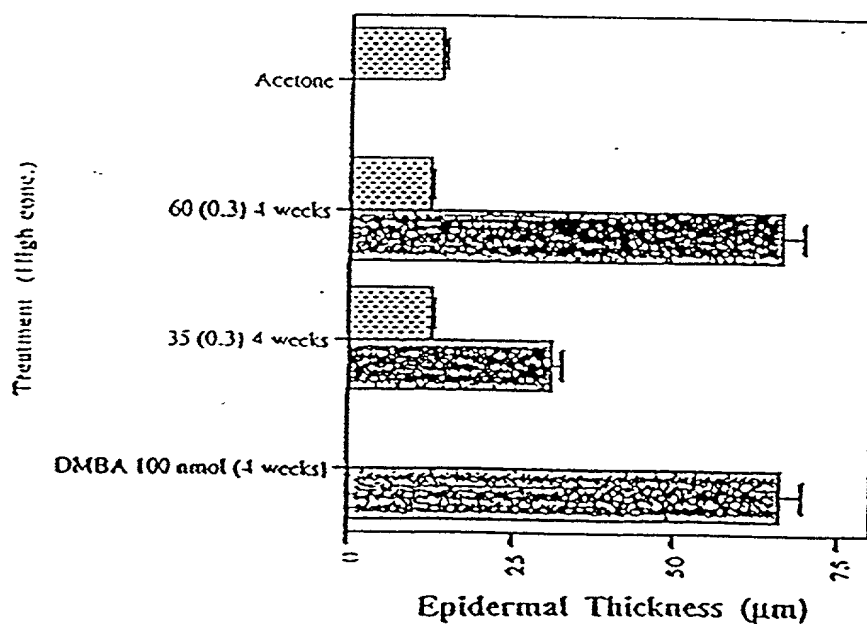


FIG. 11B

□ -DMBA

▨ +DMBA

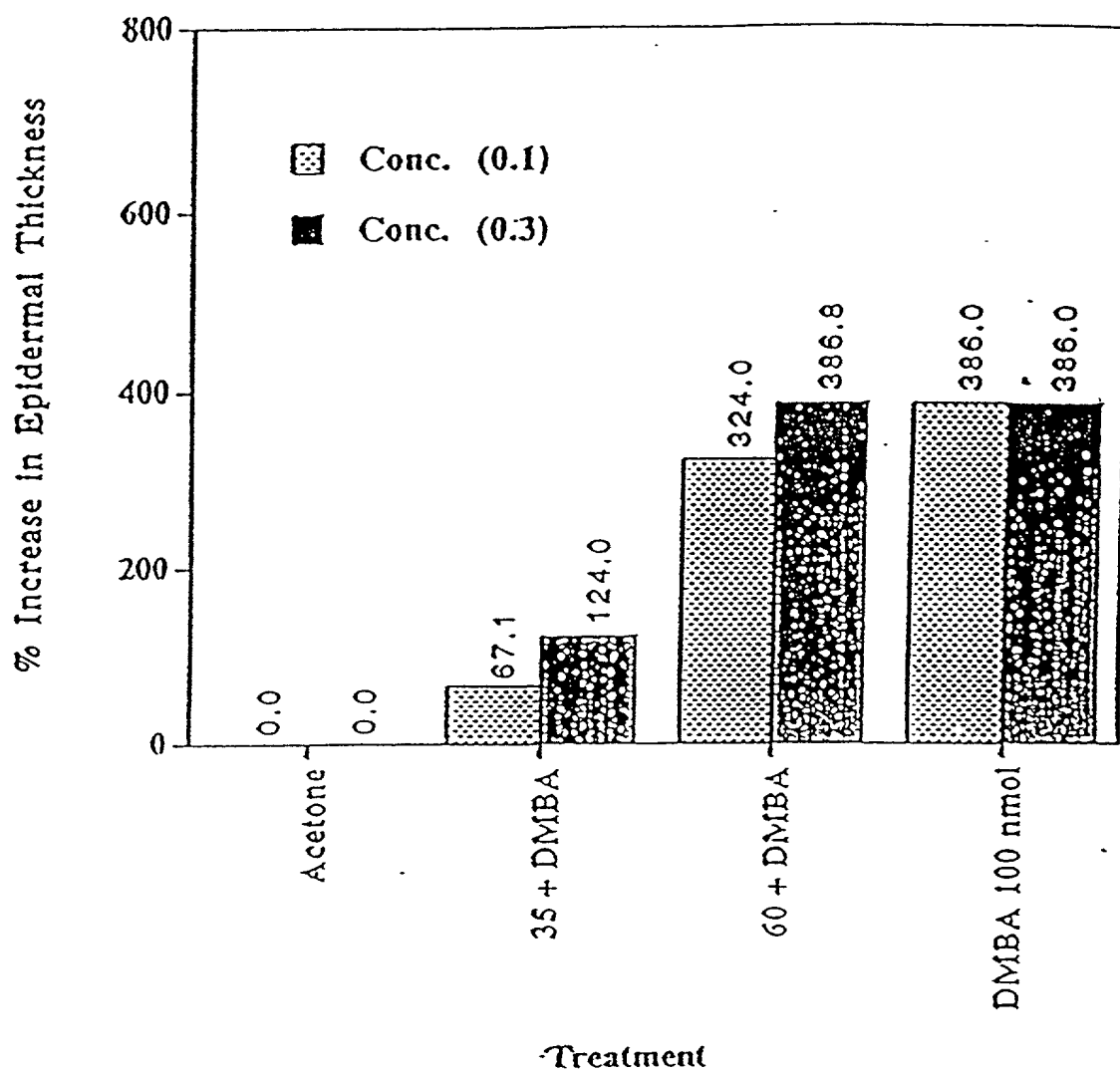


FIG. 12

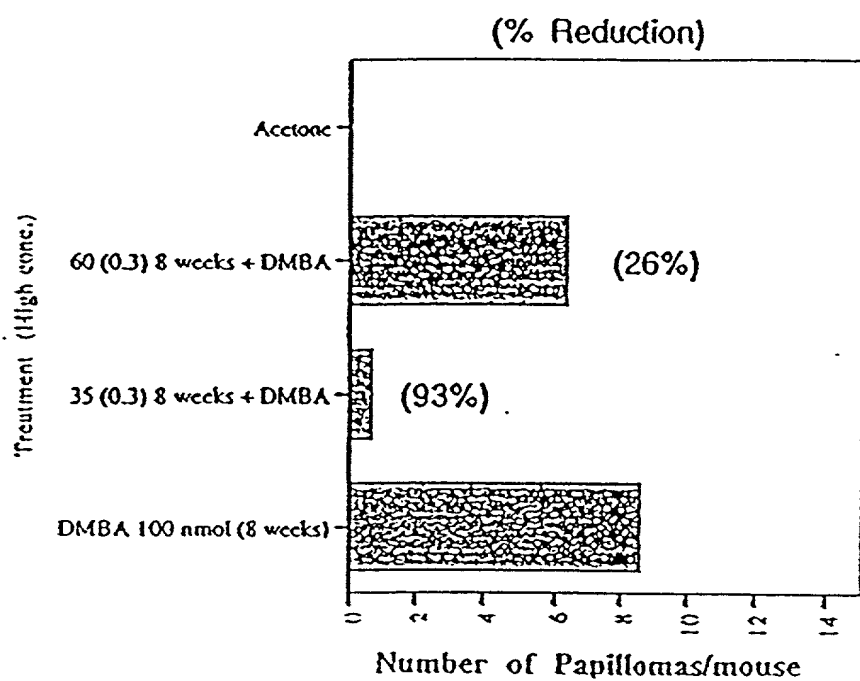


FIG. 13

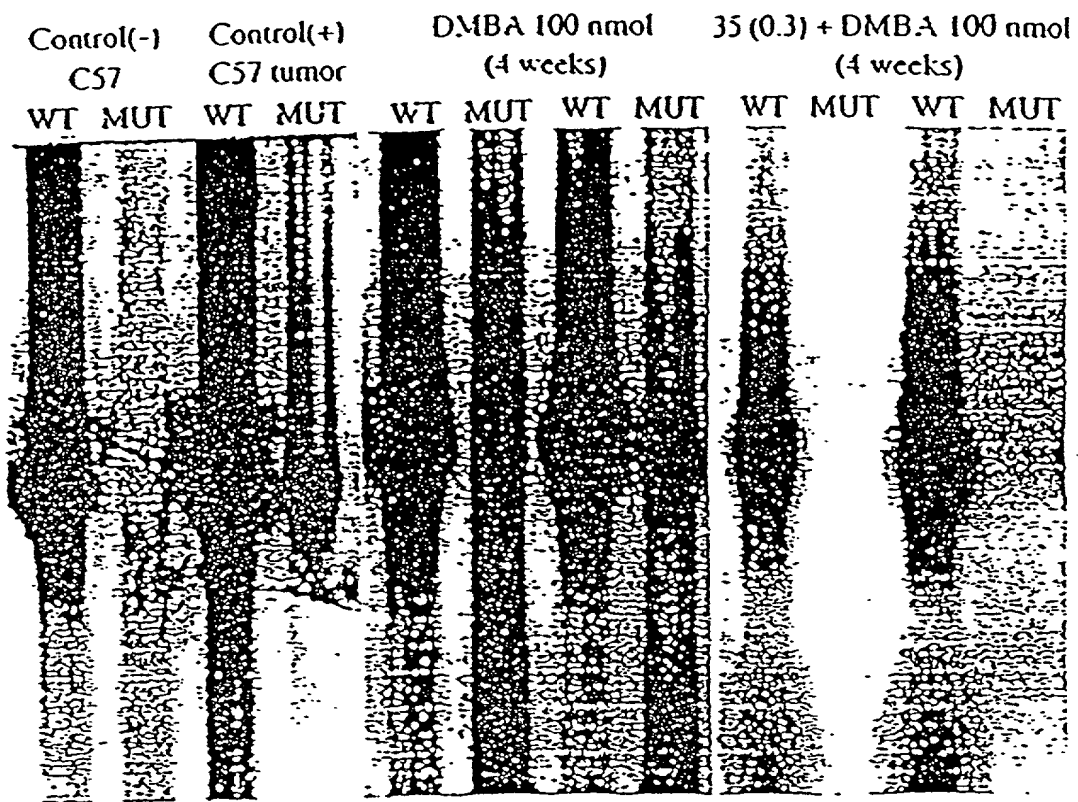


FIG. 14

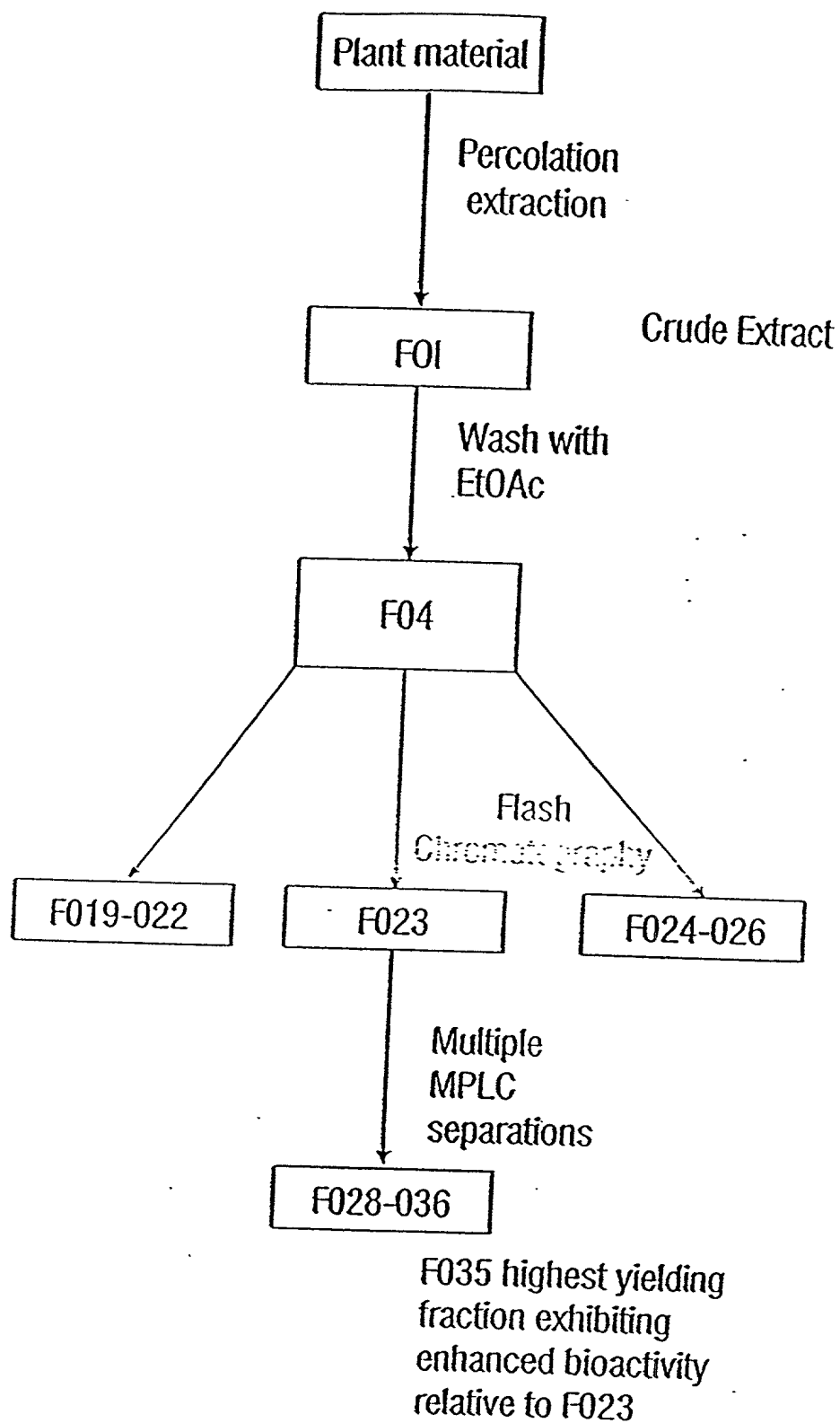


FIG. 15

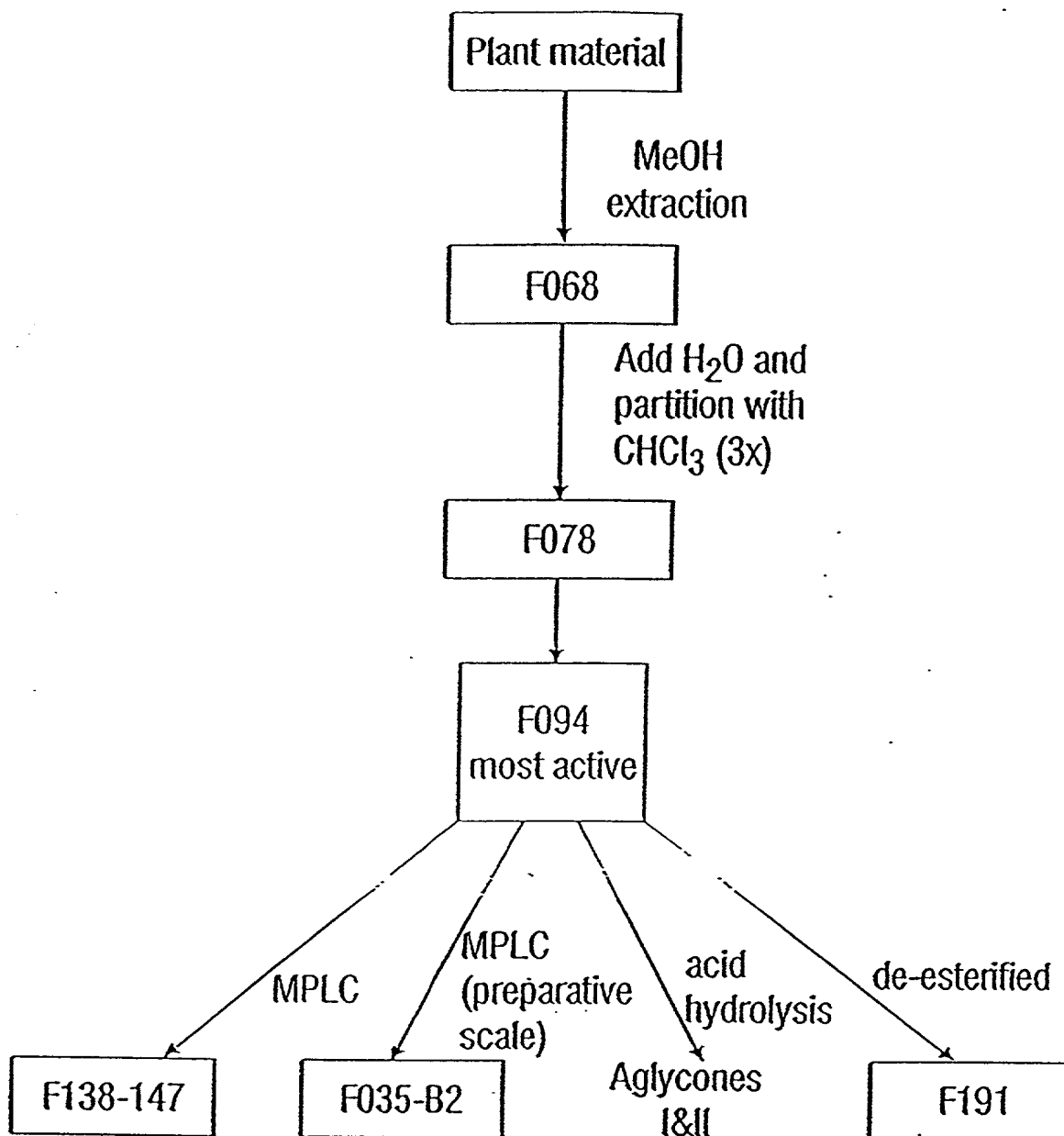


FIG. 16

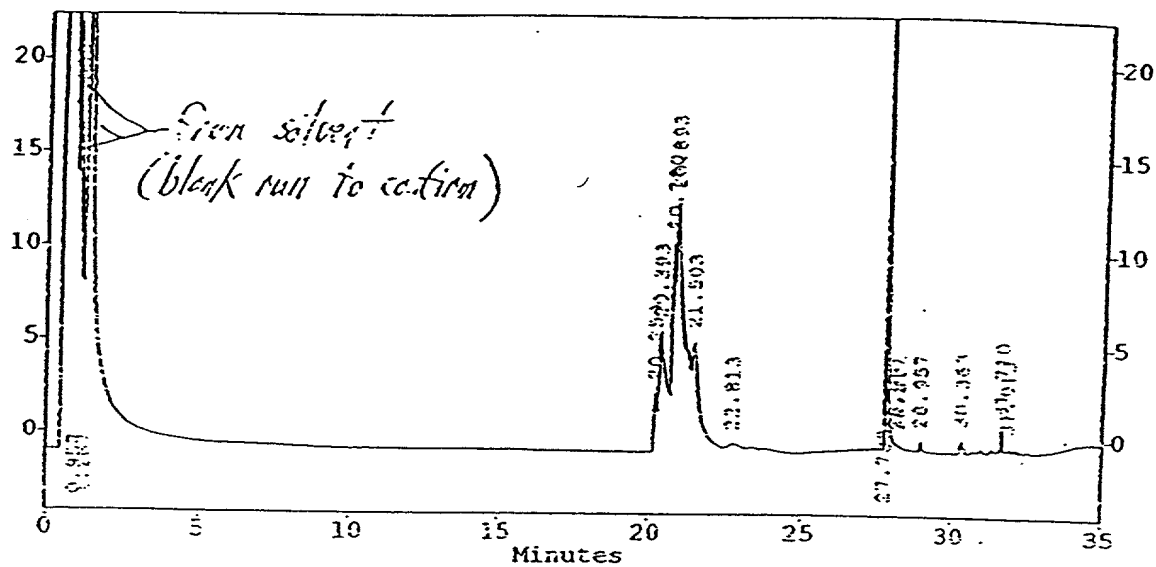


FIG. 17A

m
v

FIG. 17B

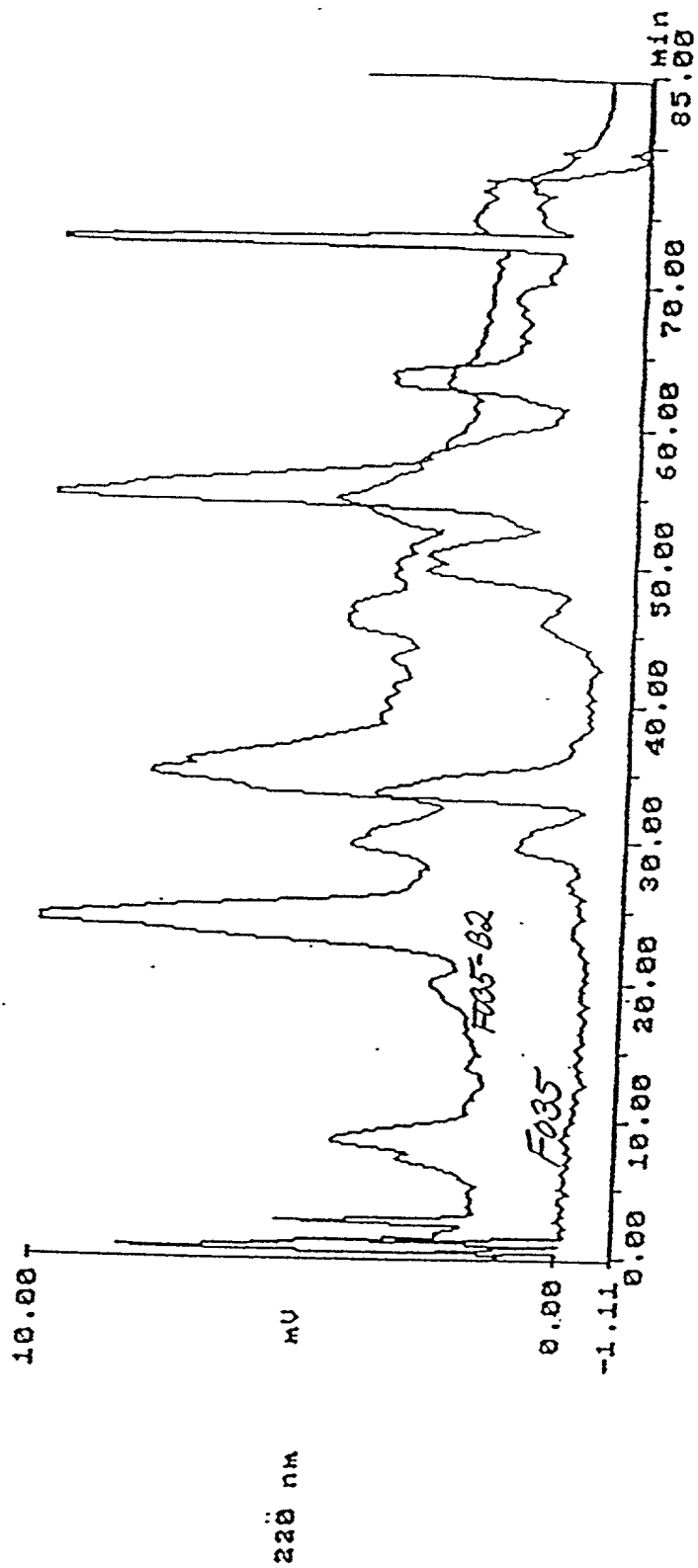


FIG. 18A

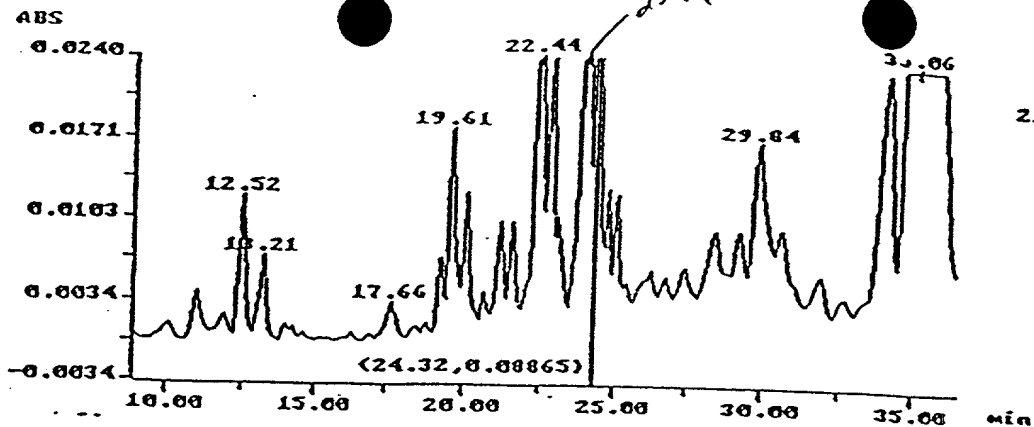


FIG. 18B

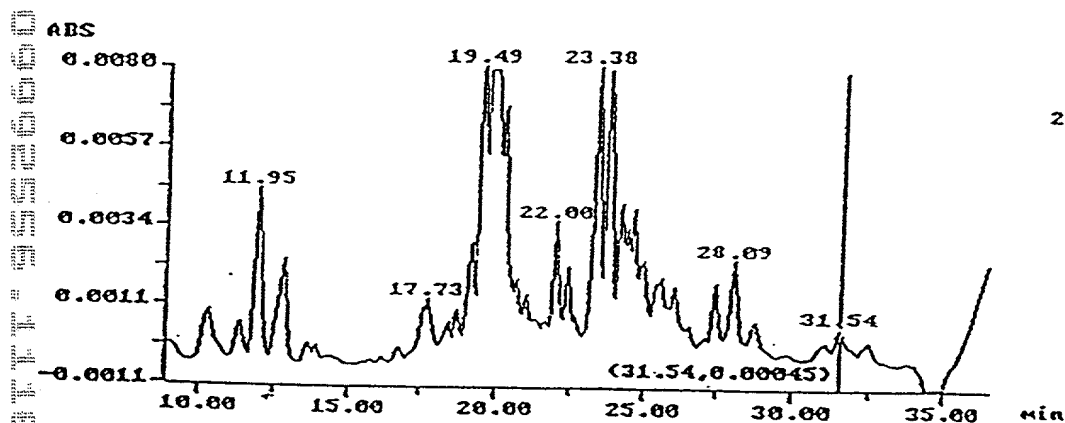


FIG. 18C

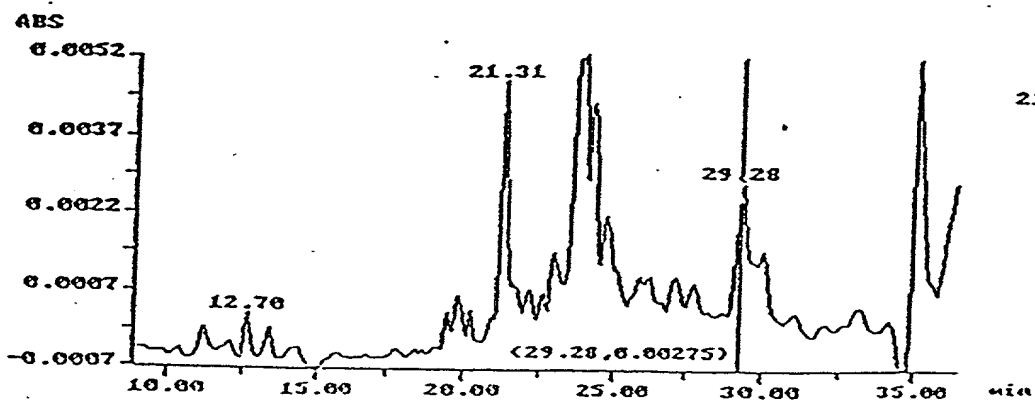


FIG. 18D

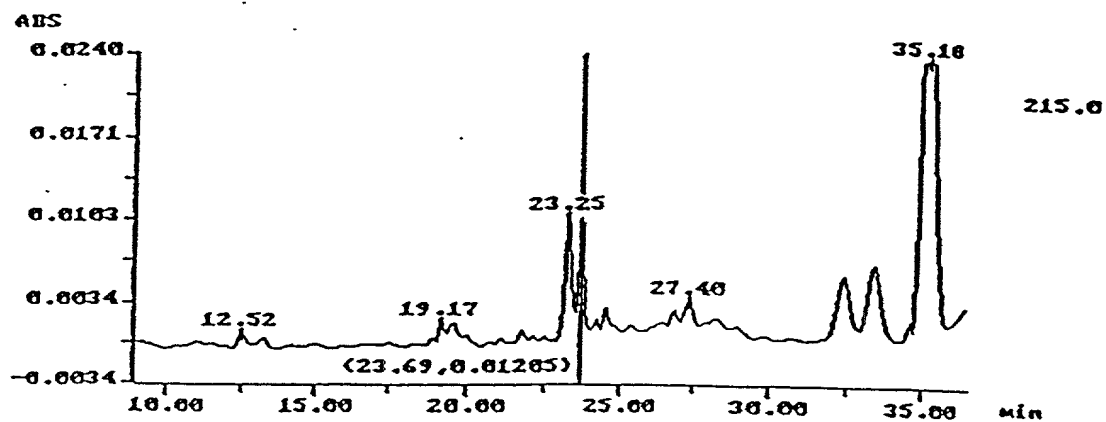


FIG. 18E

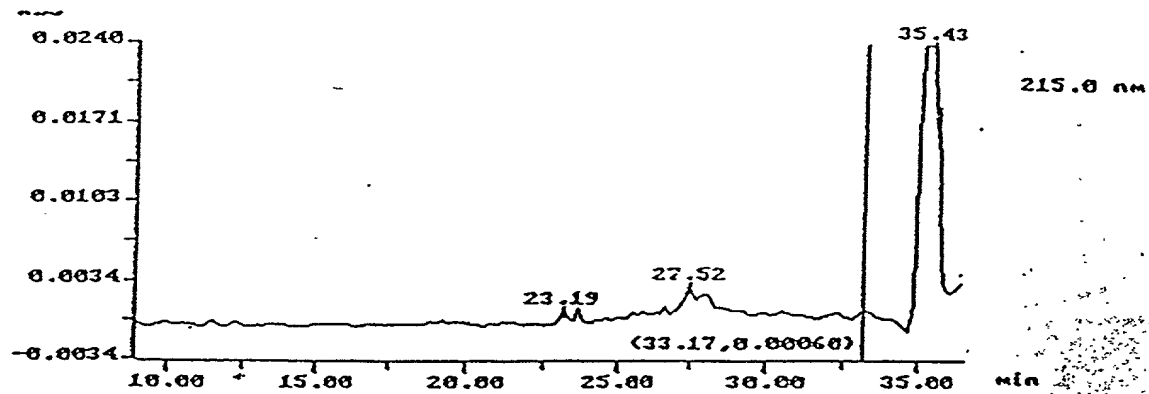


FIG. 18F

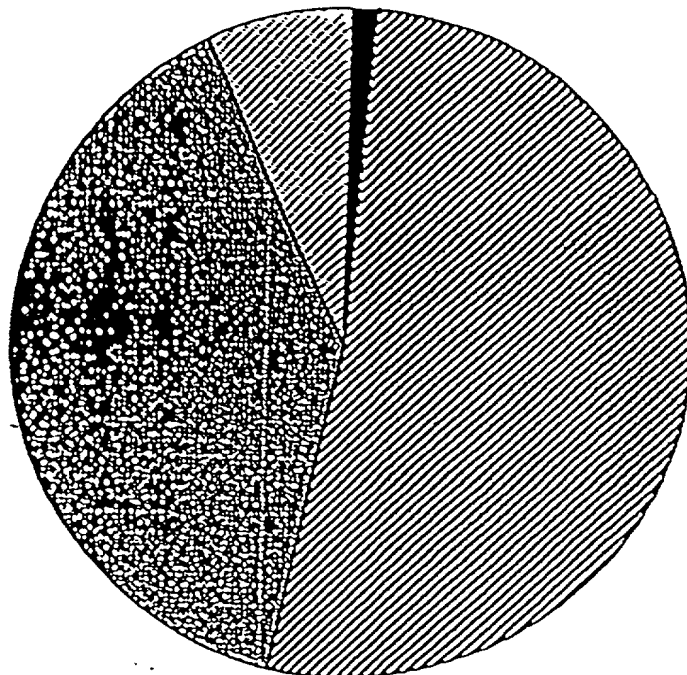


FIG. 19A

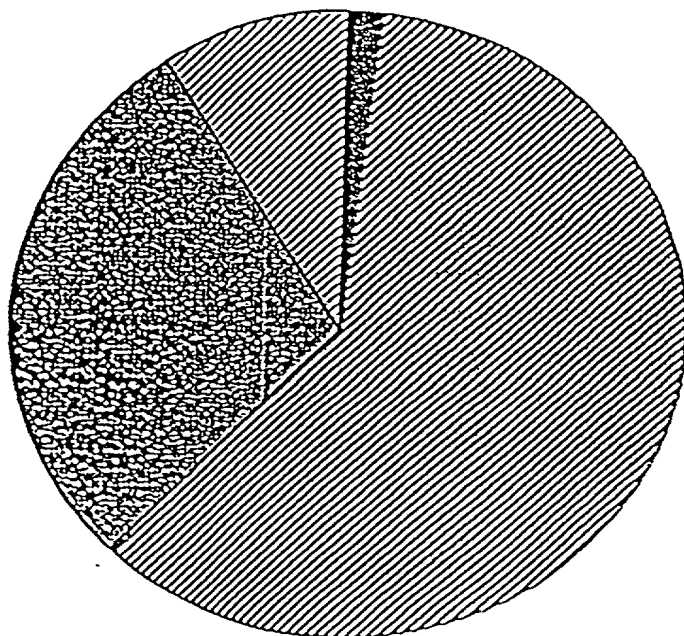
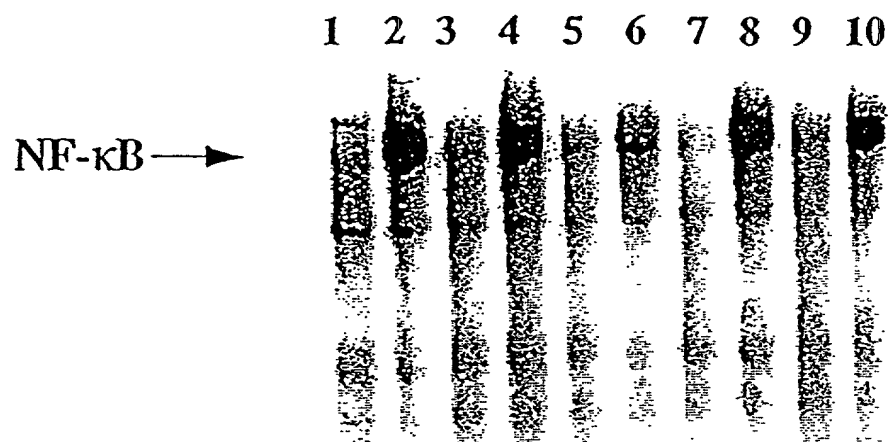


FIG. 19B



- 1 : Untreated
- 2 : TNF (100pM)
- 3 : F035 (1ug/ml)
- 4 : TNF+ F035 (1ug/ml)
- 5 : F035 (2μg/ml)
- 6 : TNF+ F035 (2μg/ml)
- 7 : F094 (1μg/ml)
- 8 : TNF+F094 (1μg/ml)
- 9 : F094 (2ug/ml)
- 10 : TNF+ F094 (2ug/ml)

FIG. 20

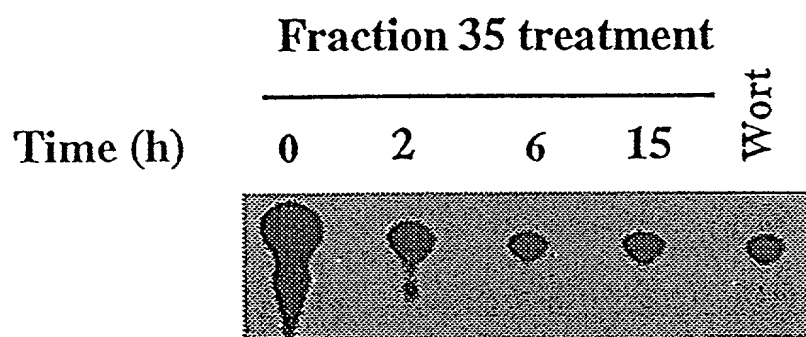


FIG 21

109111 9996660

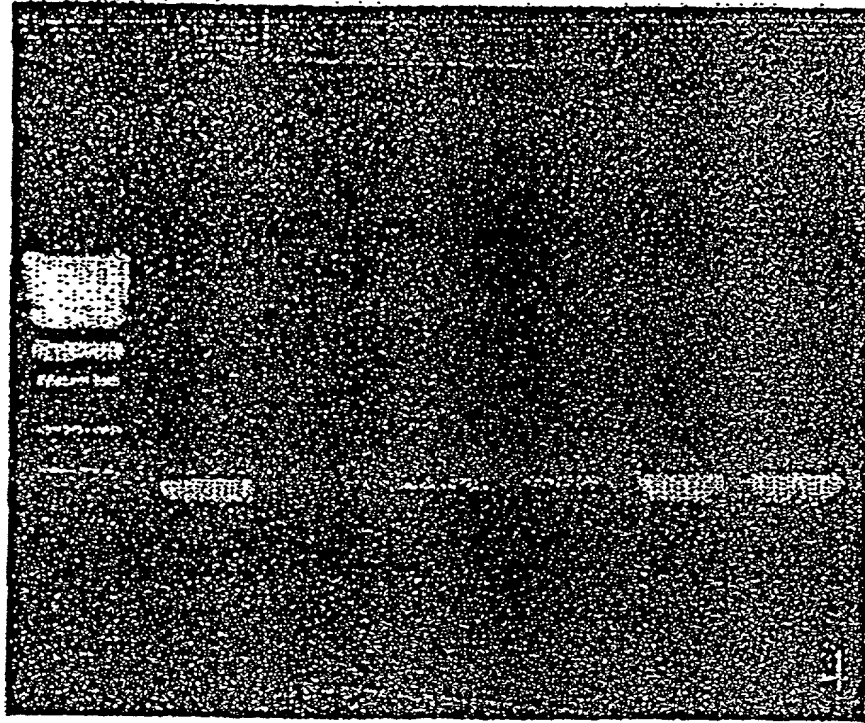


FIG 23

STRUCTURE OF ELLIPTOSIDES:

ELLIPTOSIDE E if R=OH

ELLIPTOSIDE A if R=H

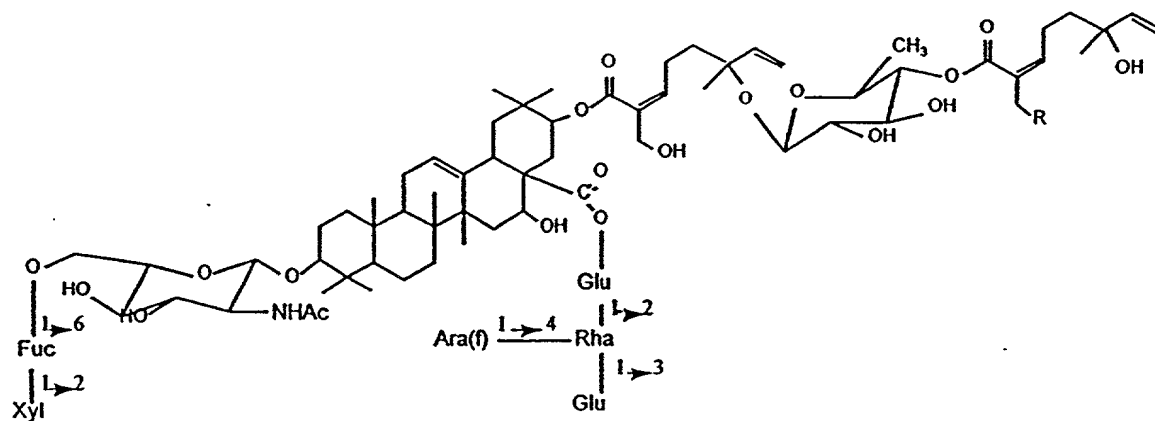
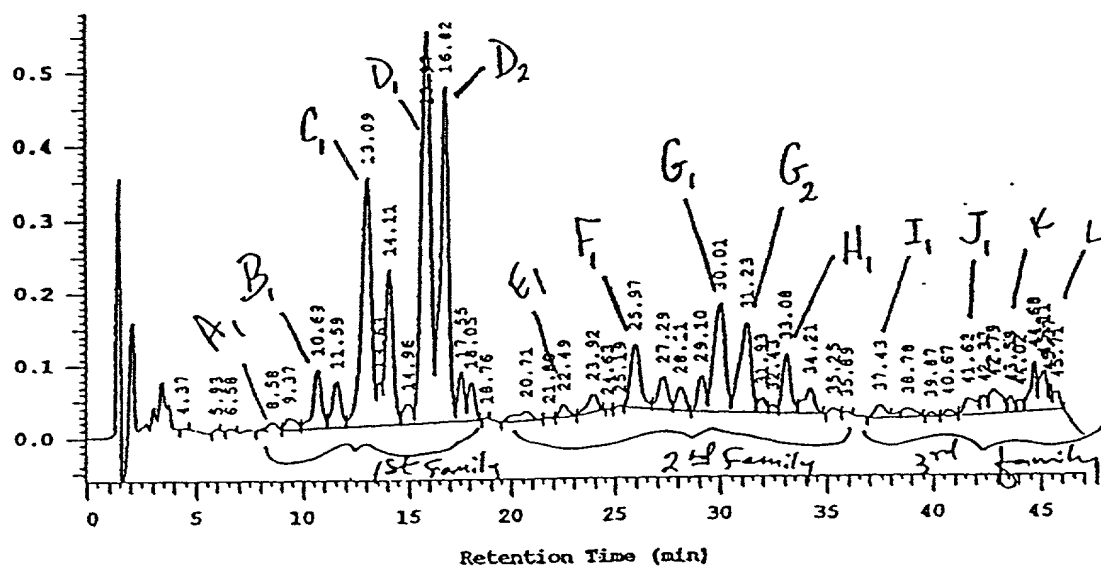


FIG 24

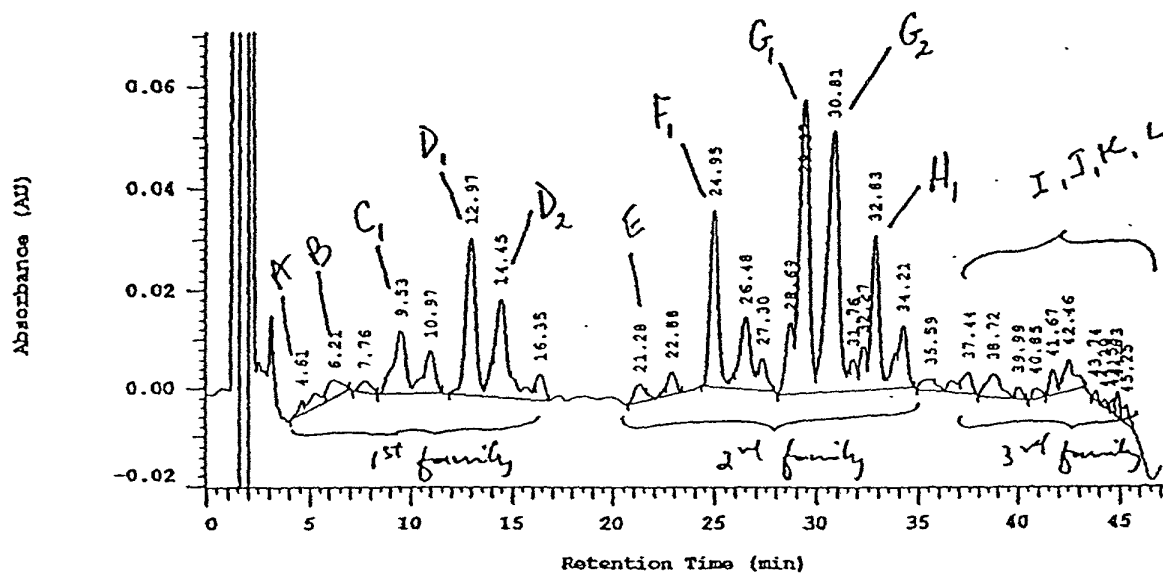
Abstracts (AU)



HPLC separation of the constituents in F094

FIG 25

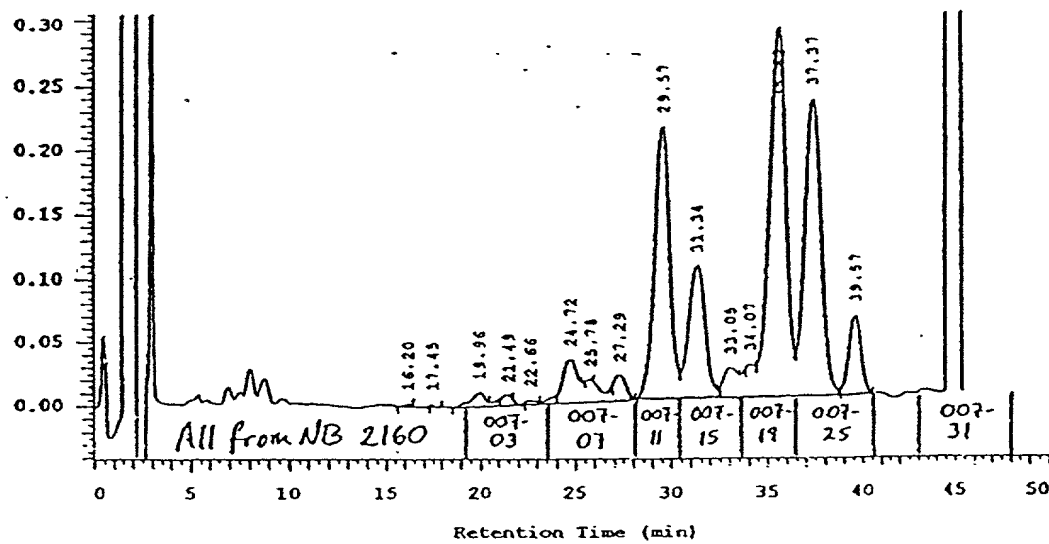
FIG 26



HPLC separation of the constituents in F035

FIG 26

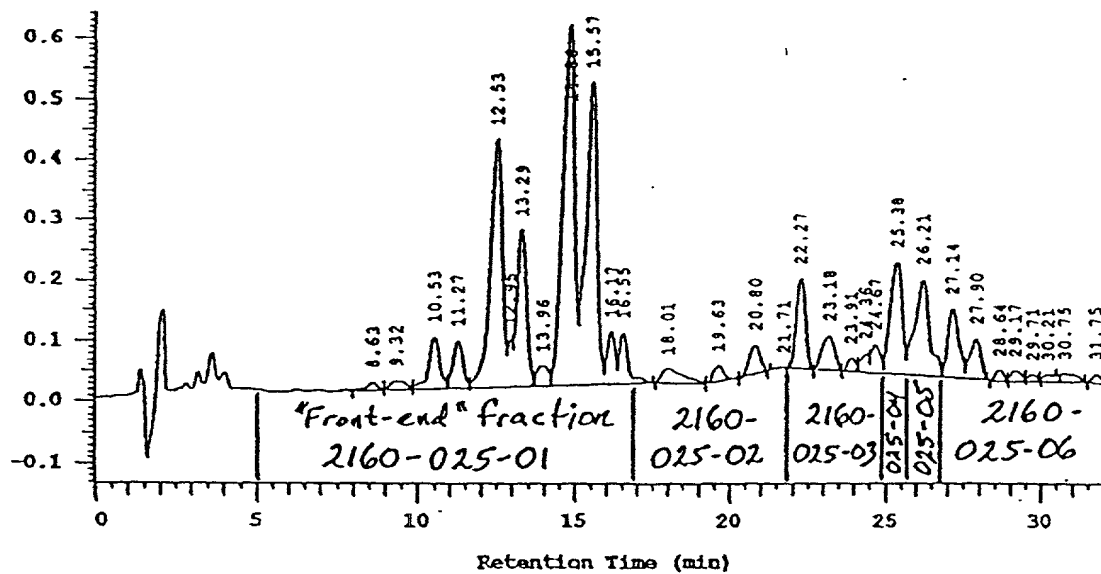
Absorbance (AU)



First Fractionation by Semi-Prep HPLC of F094

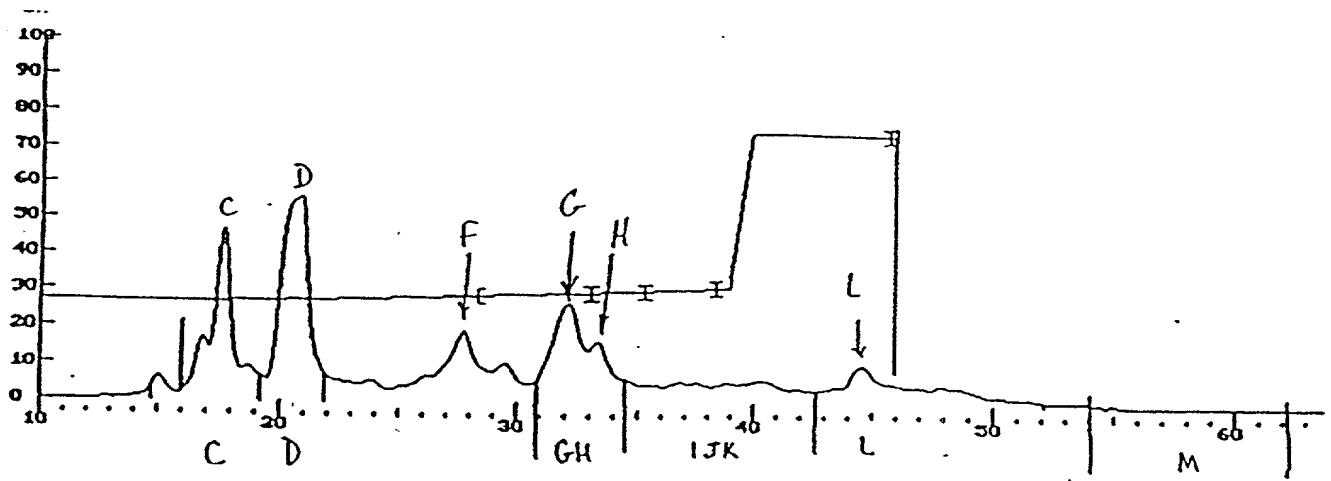
FIG 27

Absorbance (AU)



Second Fractionation by Semi-Prep HPLC of F094

FIG 28



Prep Fractionation of F094

FIG 29

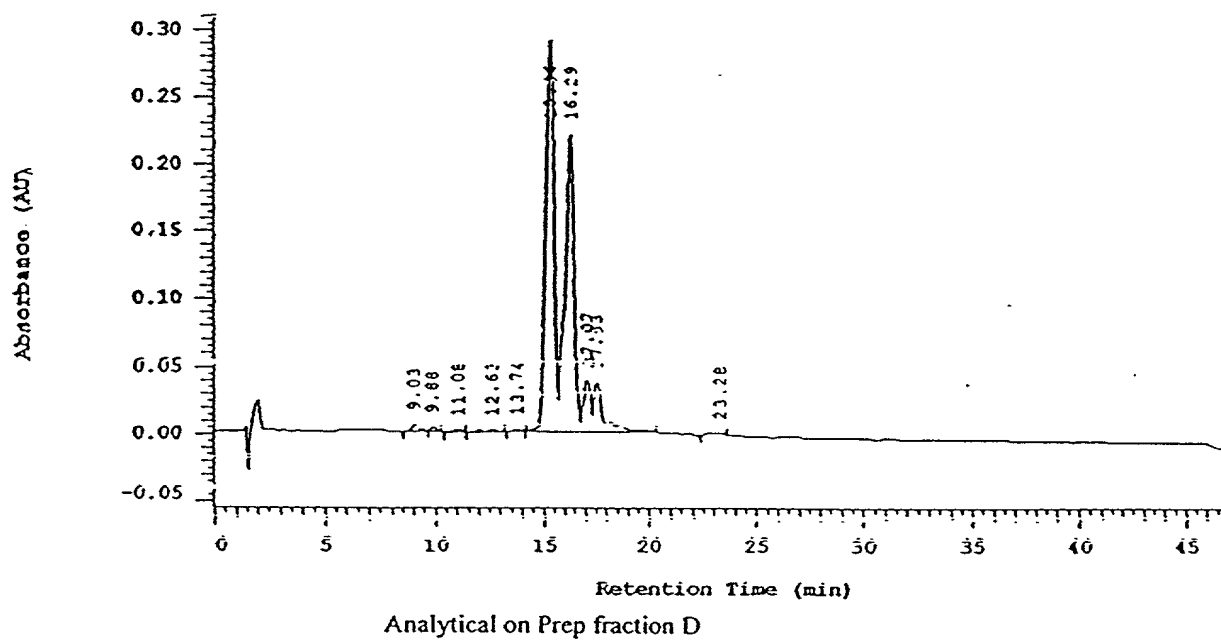
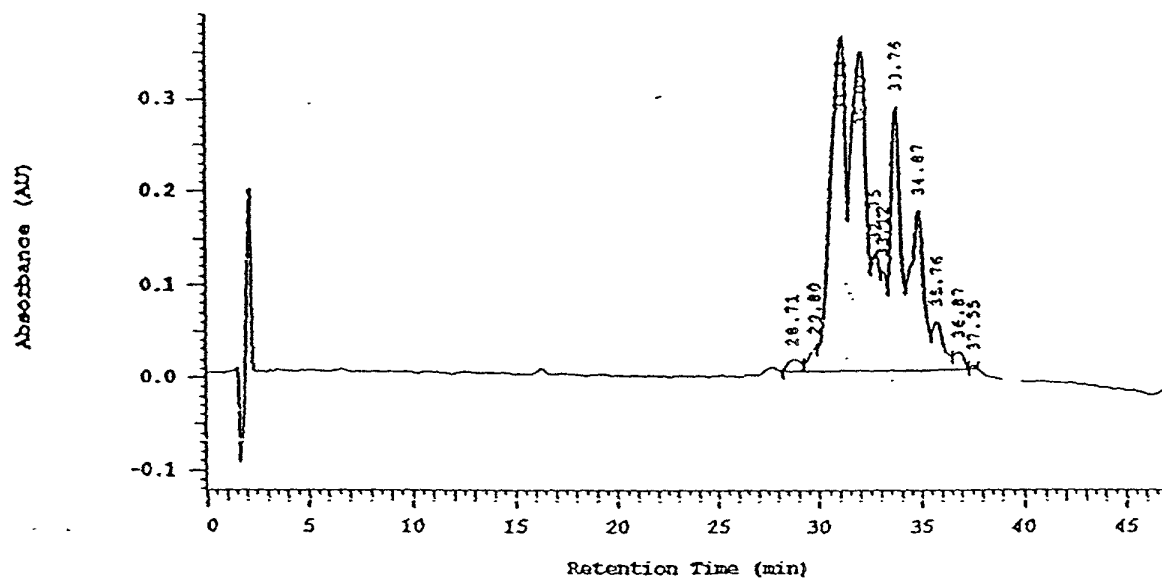
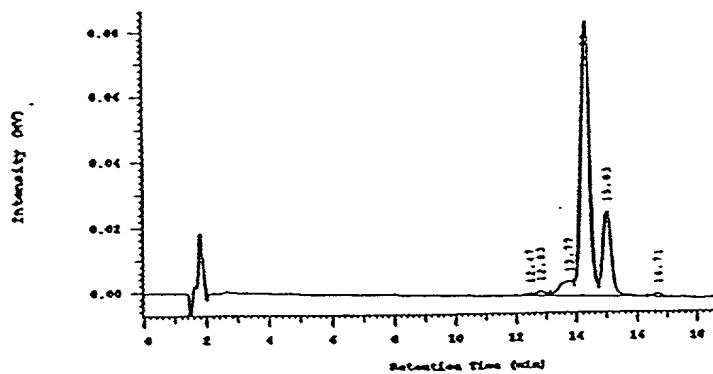


FIG 30



Analytical on Prep fraction G/H

FIG 31

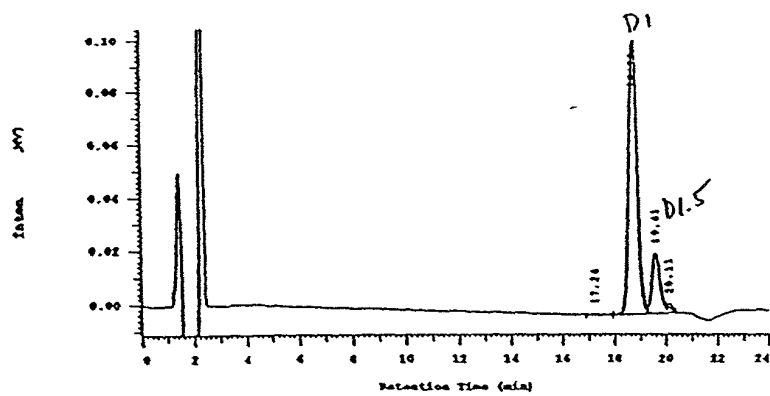


. G1 after second PFP column purification.

FIG 32

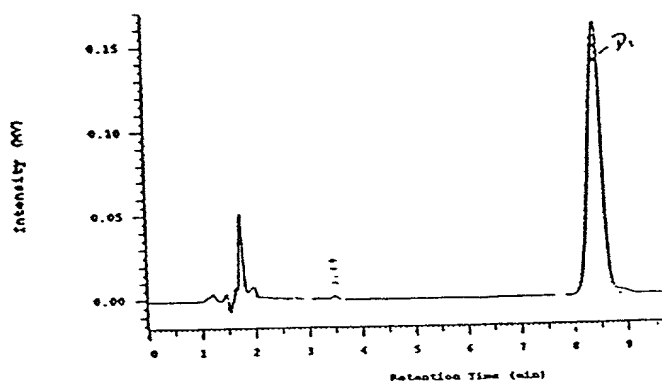
G1 after final C-18 purification

FIG 33



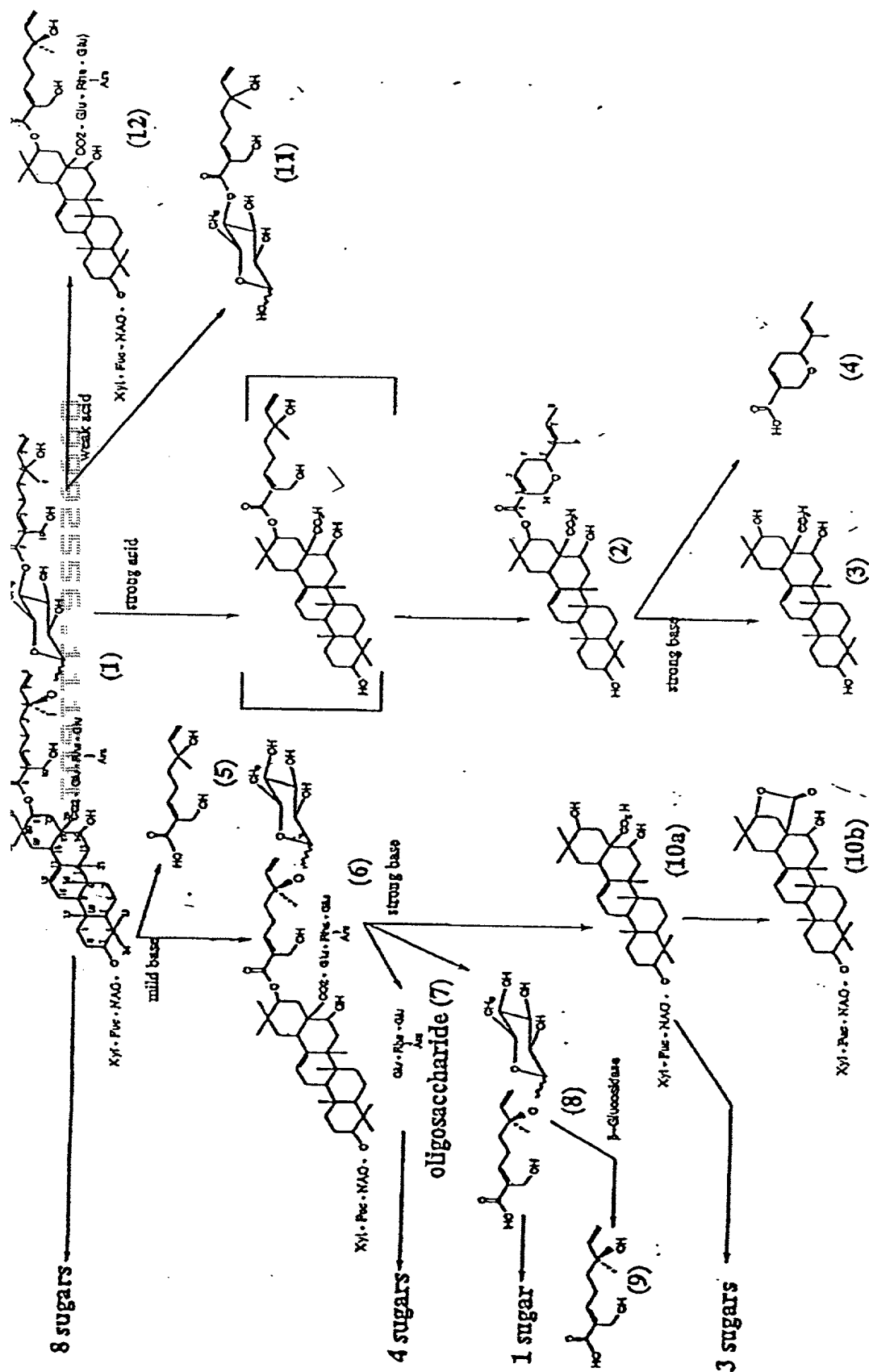
D1 after Waters C-18 column purification.

FIG 34



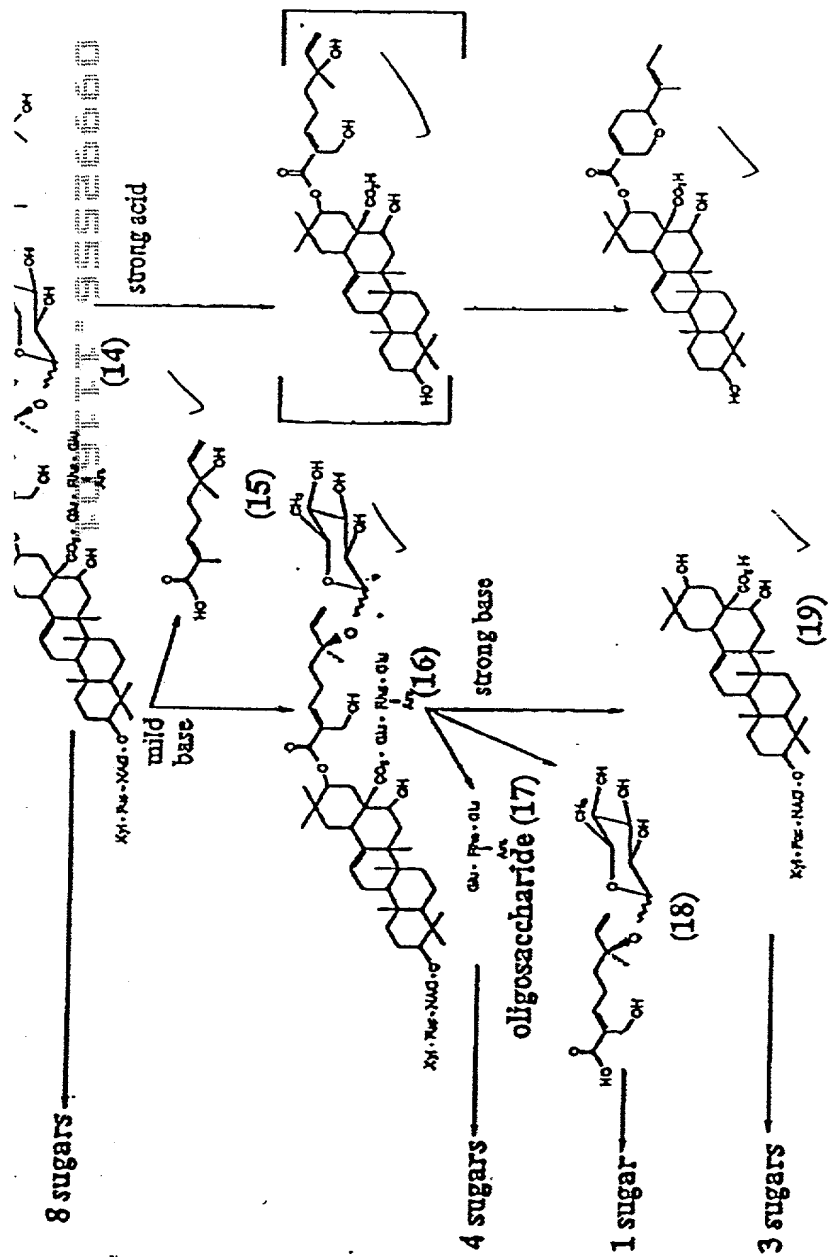
D1 after final C18-Aq purification

FIG 35



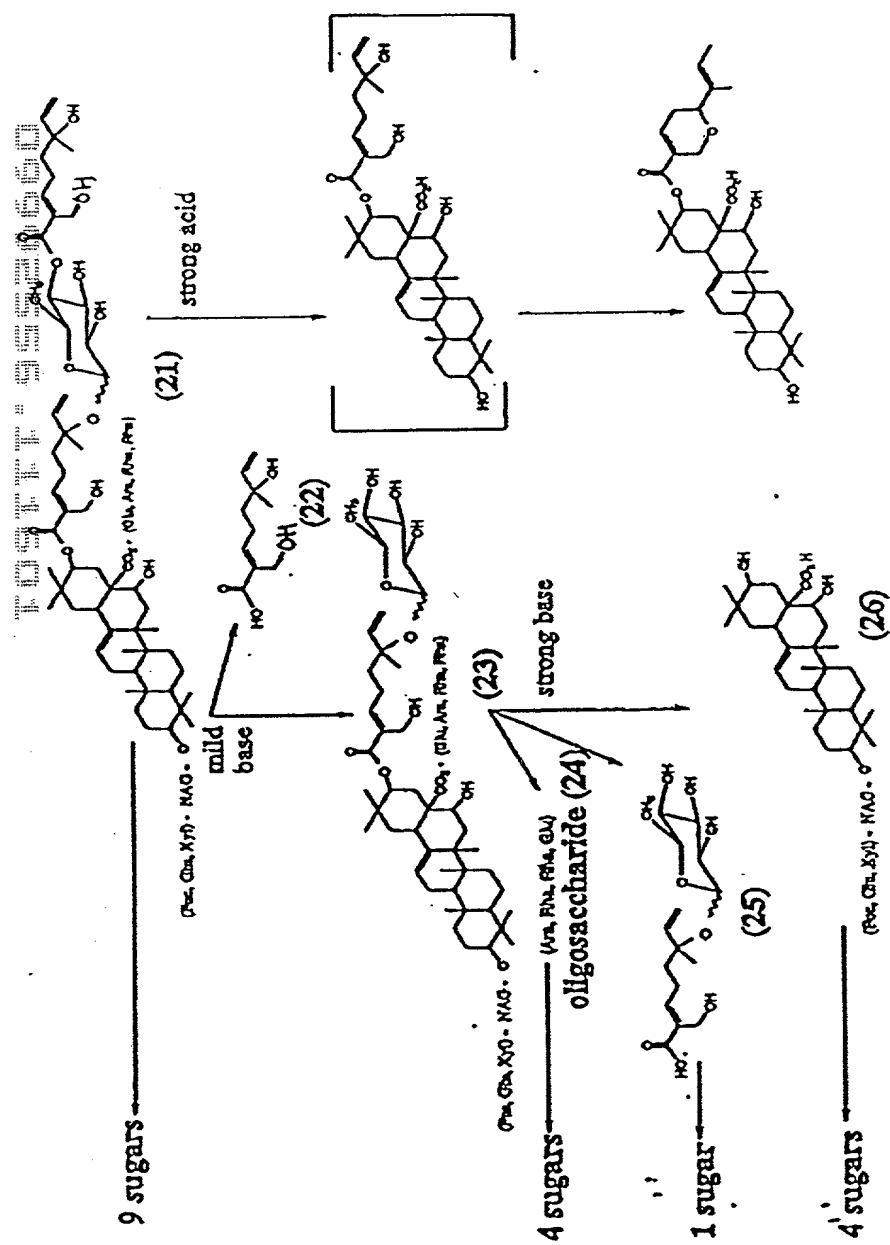
Compounds from the Degradation of D1

FIG 36



Compounds from the Degradation of G1

FIG. 37



Compounds from the Degradation of B1

85
G
—
L

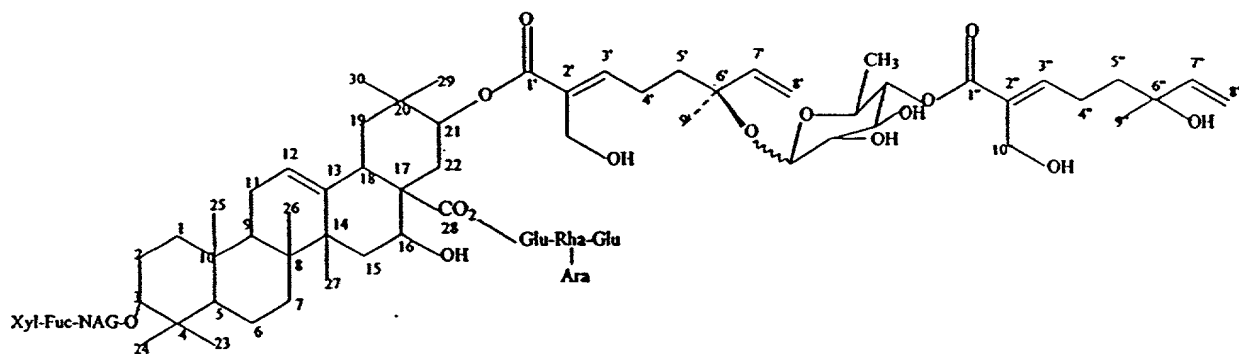


FIG. 39

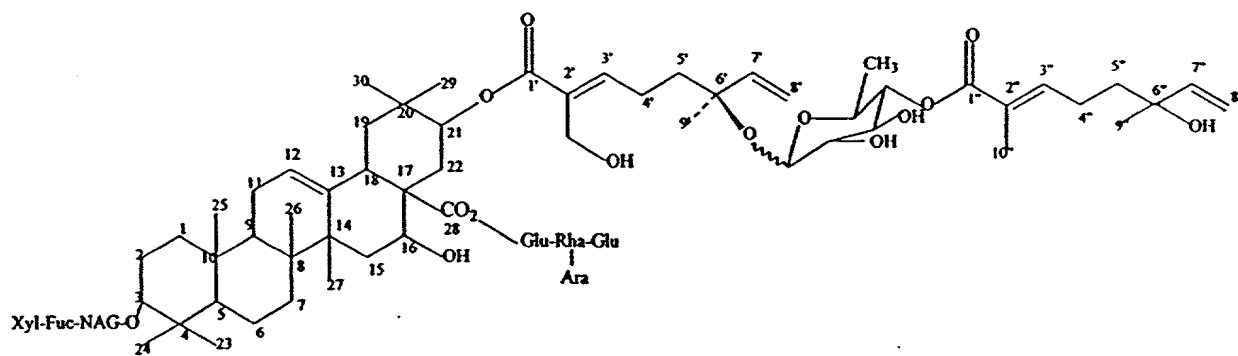


FIG. 40

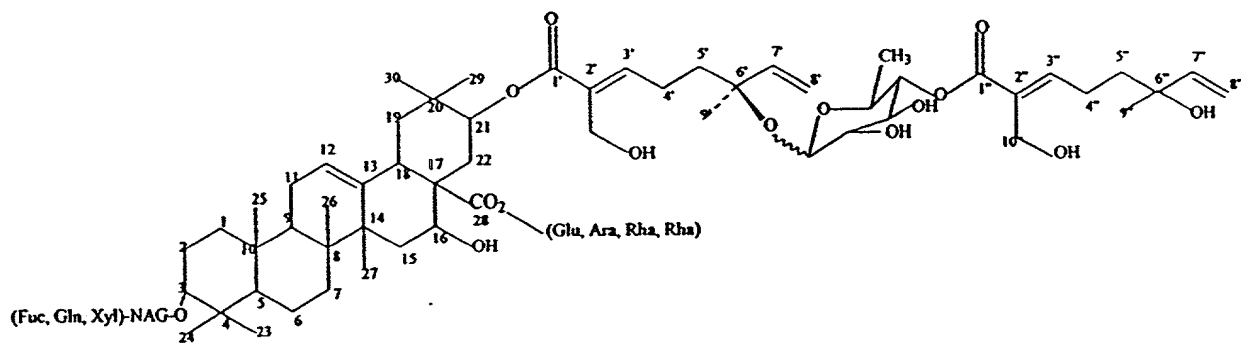
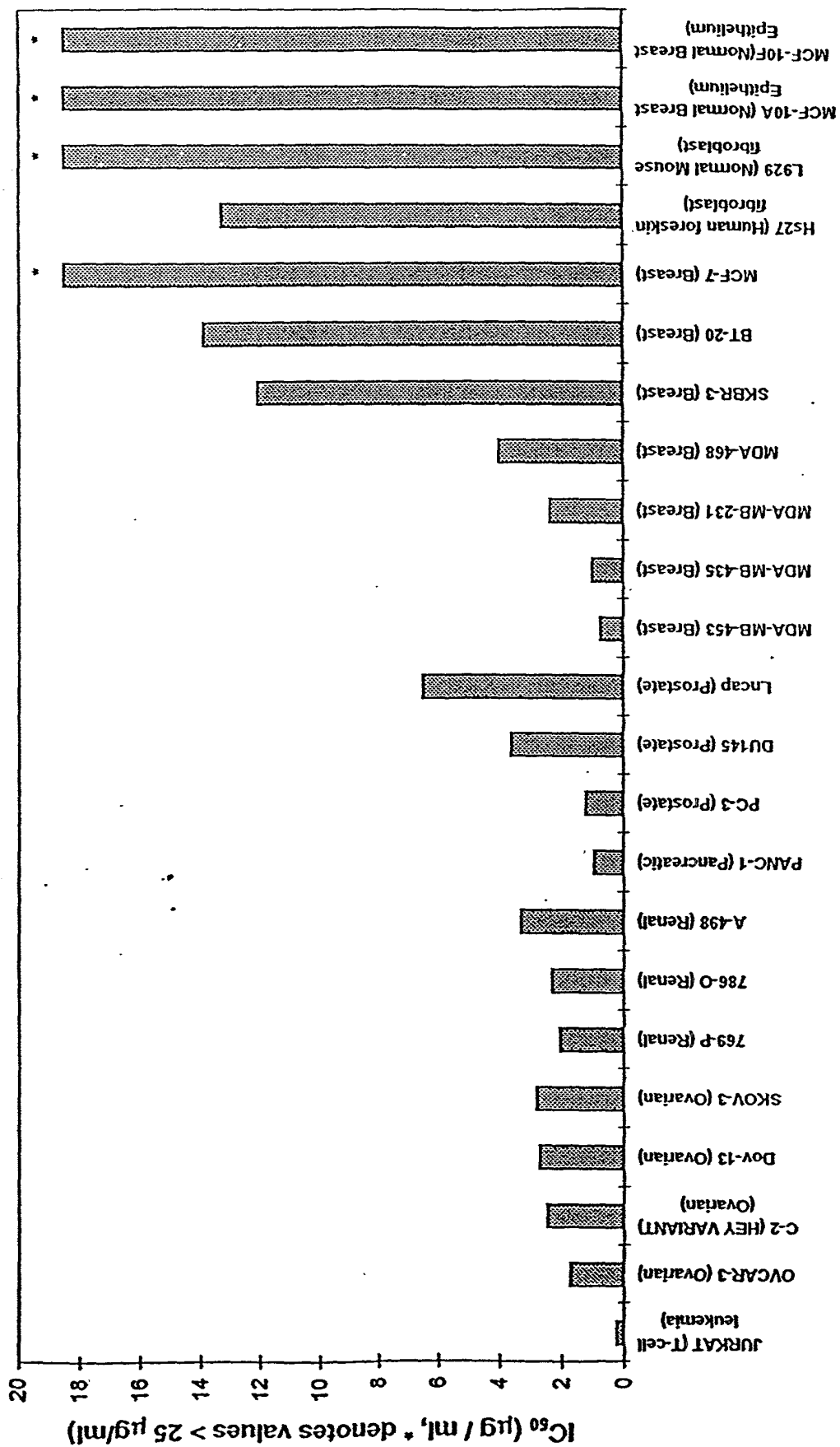


FIG. 41



Cell Lines

FIG. 42

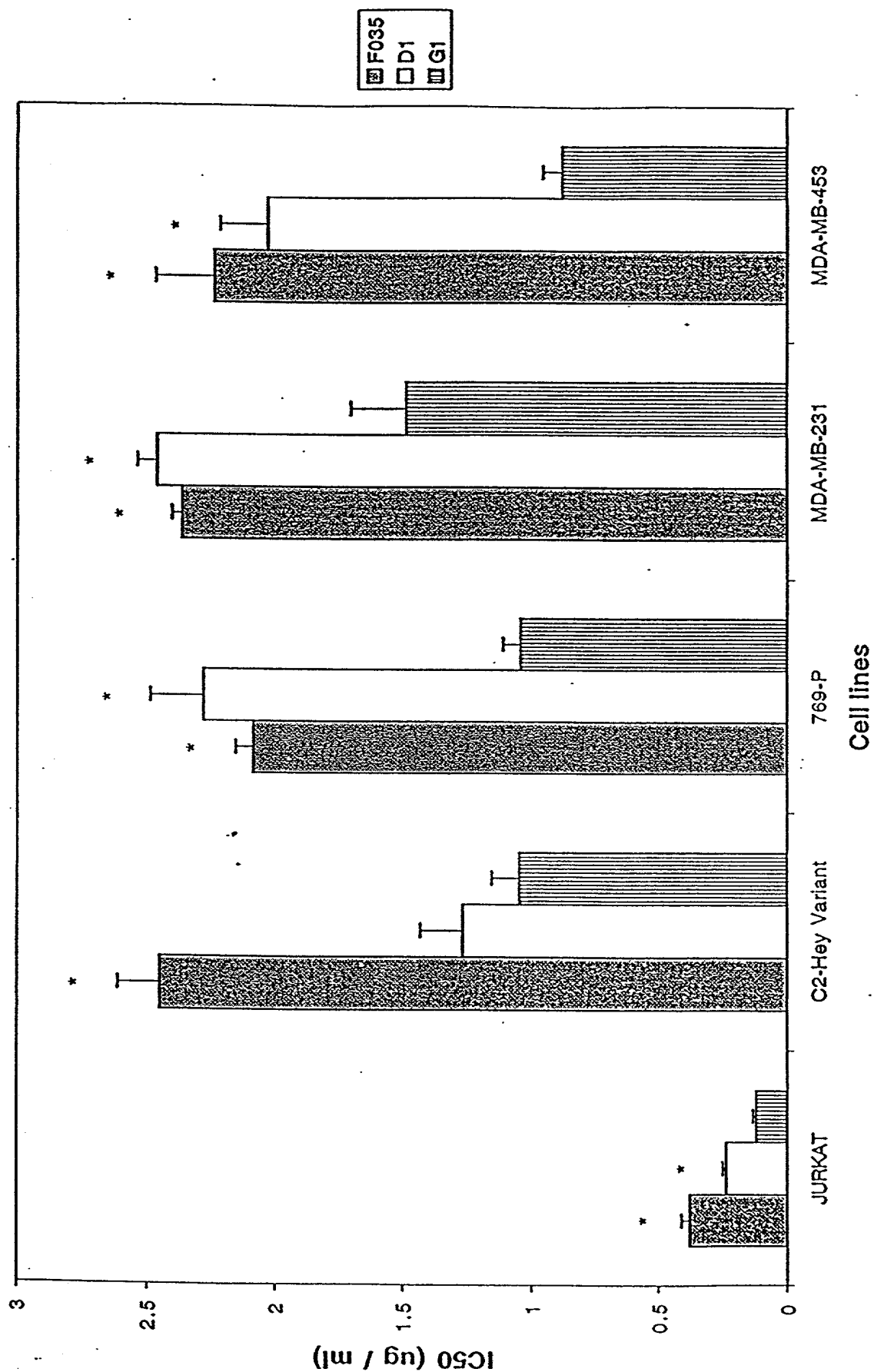
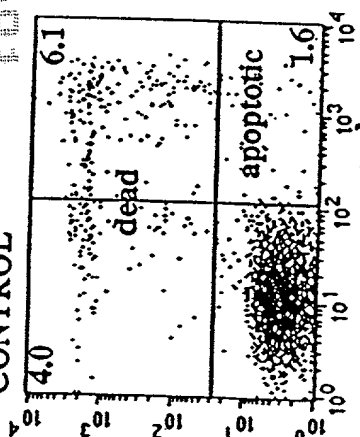


FIG 43

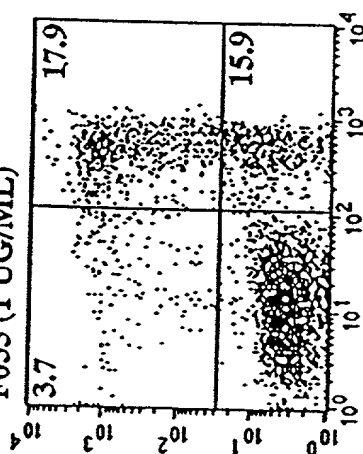
CONTROL

TOPT 992660

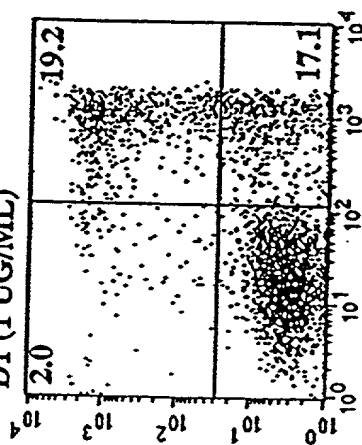
PI



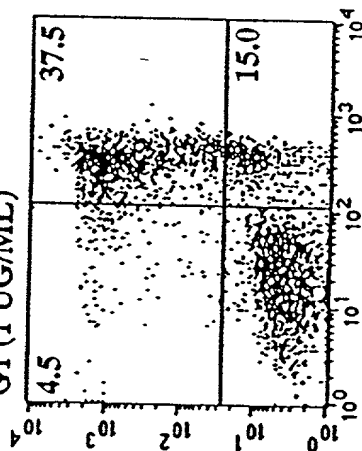
F035 (1 UG/ML)



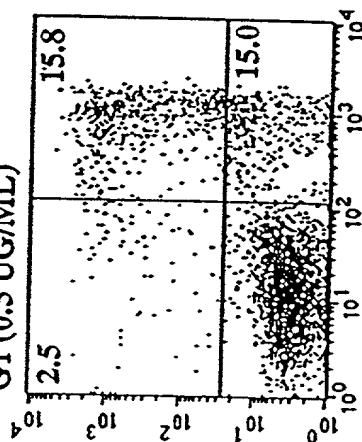
D1 (1 UG/ML)



G1 (1 UG/ML)



G1 (0.5 UG/ML)

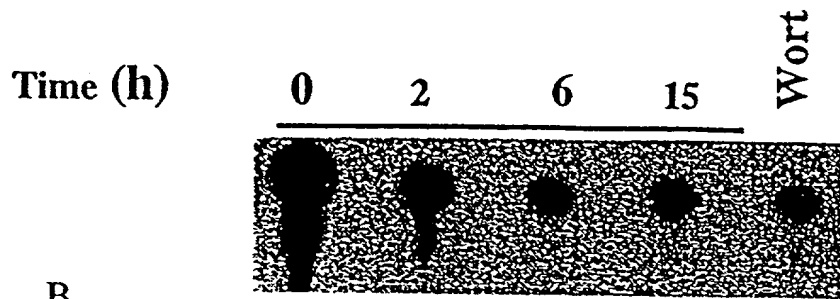


ANNEXIN-V-FITC

FIG 44

A

Fraction 35 treatment



B

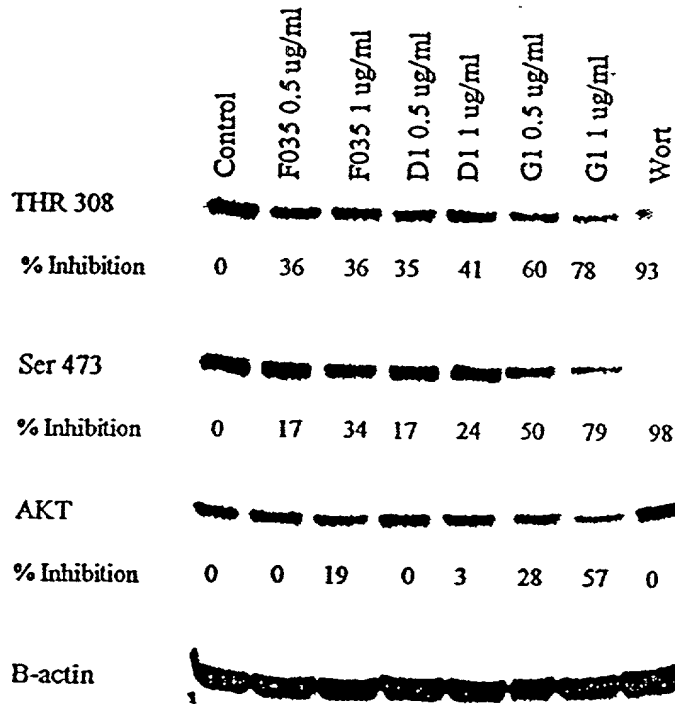
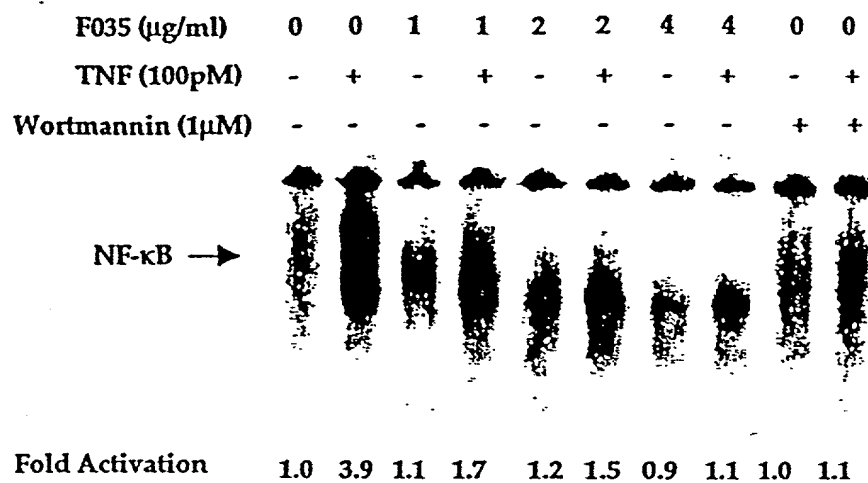
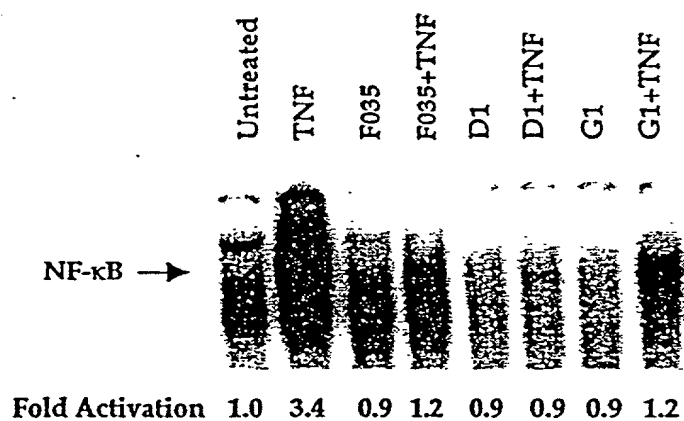


FIG 45

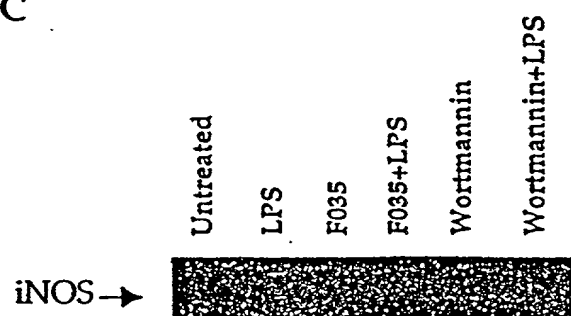
A



B



C



D

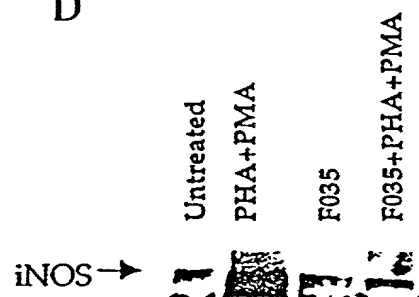


FIG 46

Effect of F035 & D1 on cleavage of PARP in Jurkat cells.

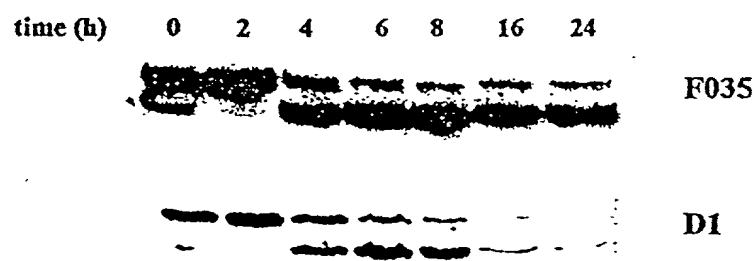


FIG 47

Effect of z-vad fmk on F035 induced PARP cleavage in Jurkat cells

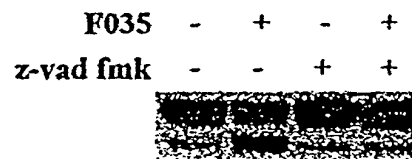


FIG 48

Effect of F035, F094, D1 & G1 on caspase activity in Jurkat cells.

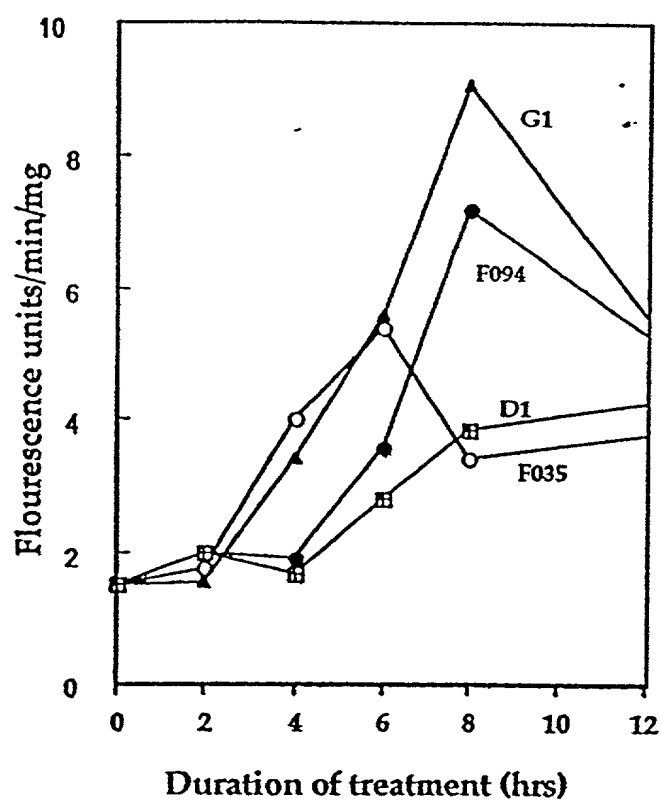


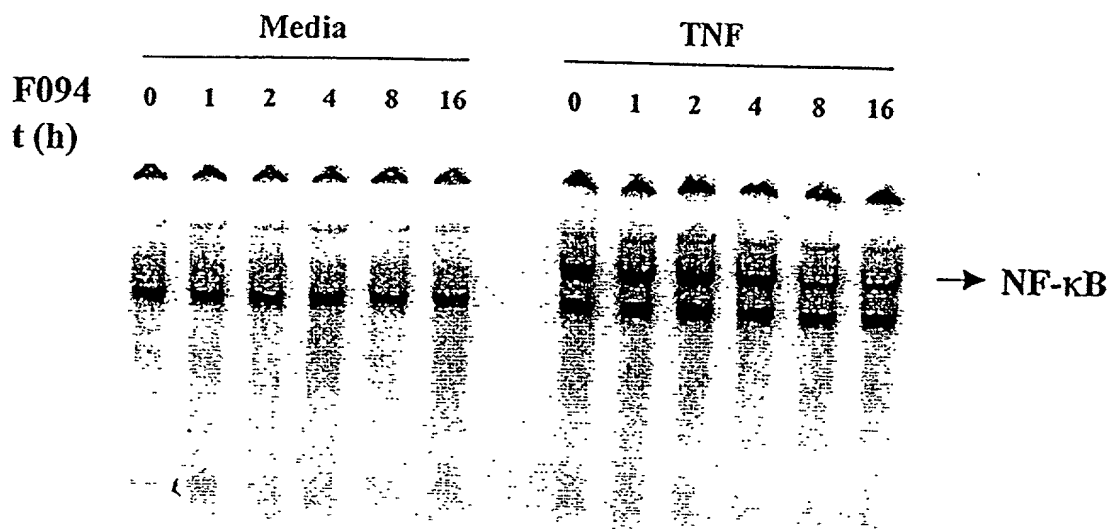
FIG 49

Effect of F035 on cytochrome c release from Jurkat mitochondria

time (h) 0 4 6
 → Cytochrome c

FIG 50

A



B

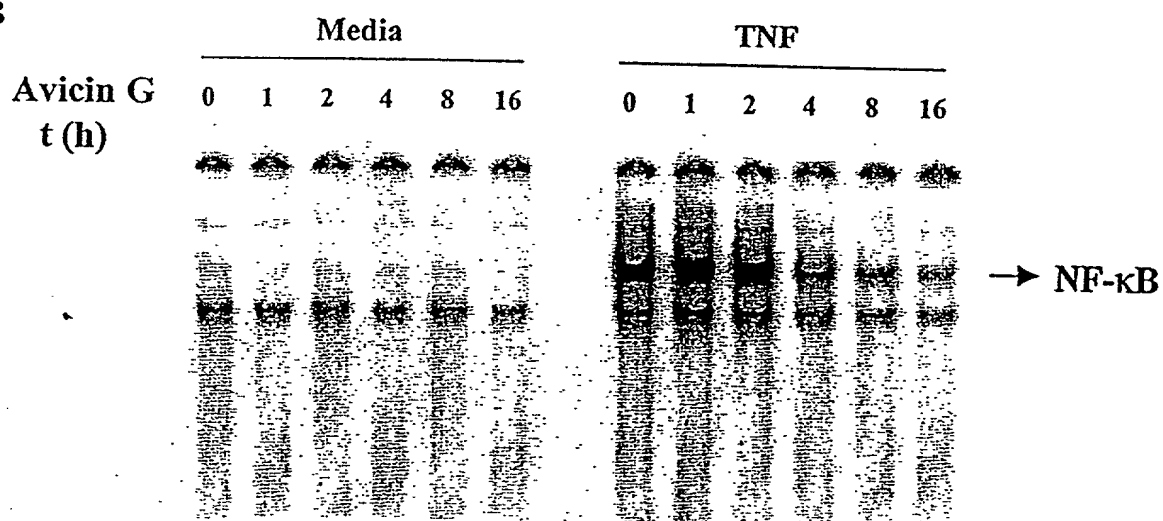
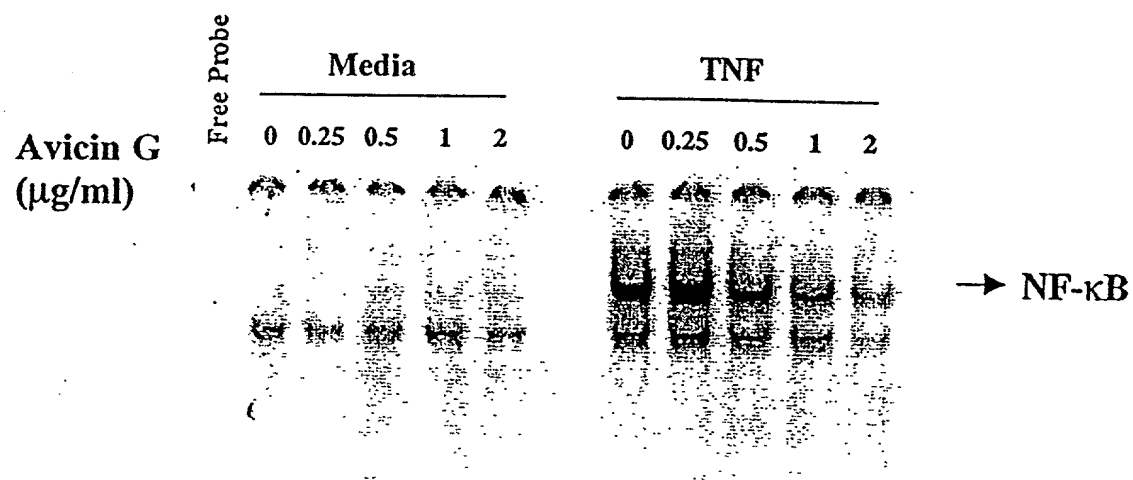


FIG. 51 A-B

A



B

Rabbit IgG	-	-	-	-	-	+
anti-p65	-	-	-	-	+	-
Cold wt	-	-	-	+	-	-
Cold mut	-	-	+	-	-	-
TNF	-	+	+	+	+	+

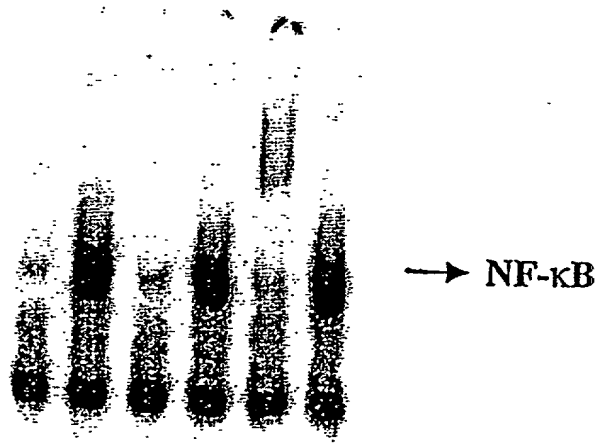


FIG. 52 A-B

A **I κ B**

Time (min) 0 2 5 10 15 30



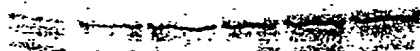
Untreated



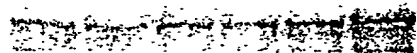
Avicin G

B **p65**

Time (min) 0 2 5 10 15 30



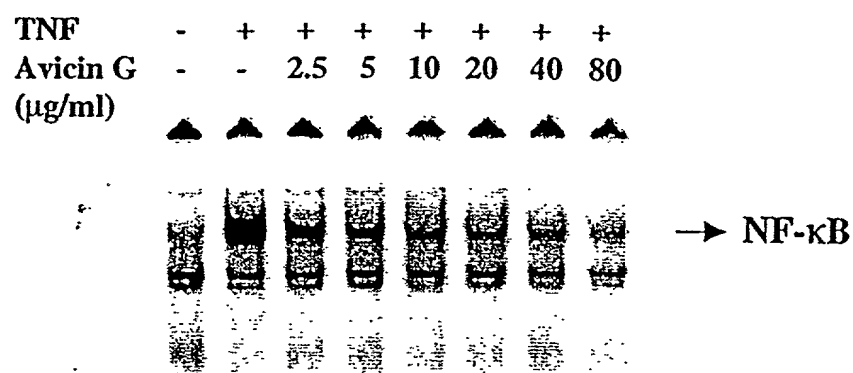
Untreated



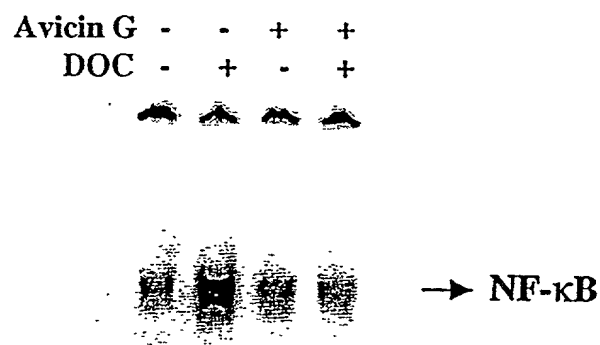
Avicin G

FIG. 53 A-B

A



B



C

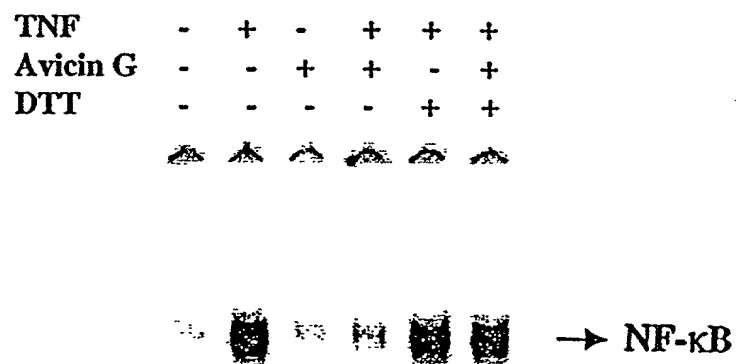
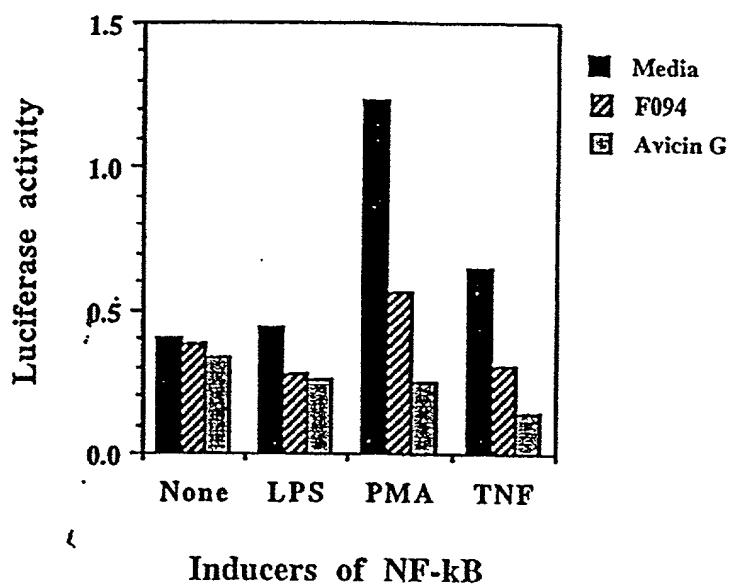


FIG. 54 A, B, C

A



B

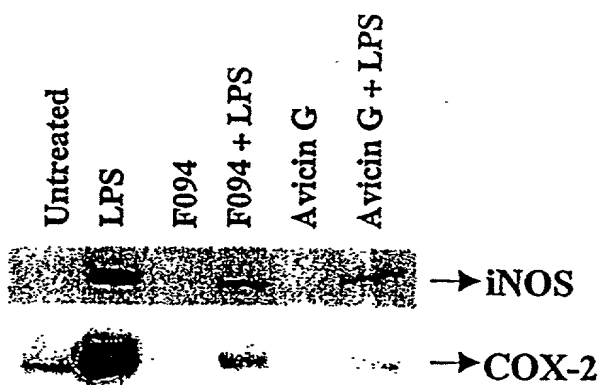
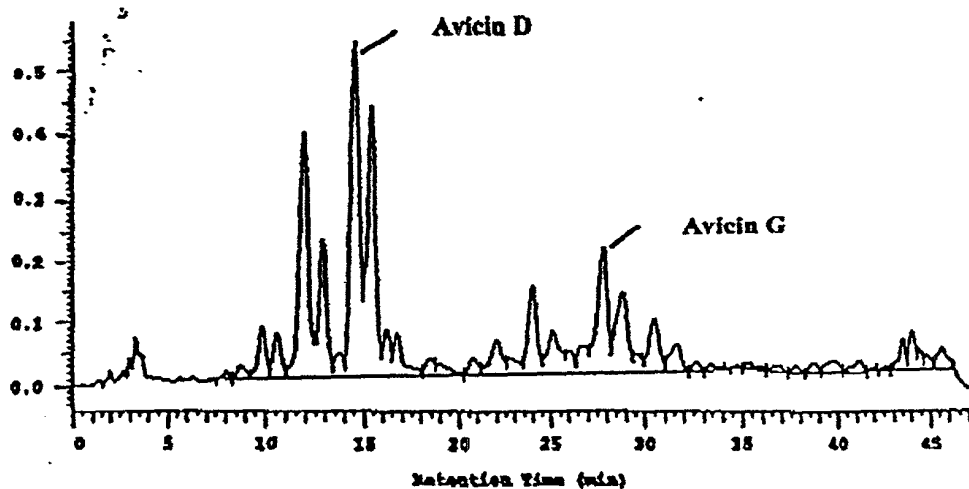


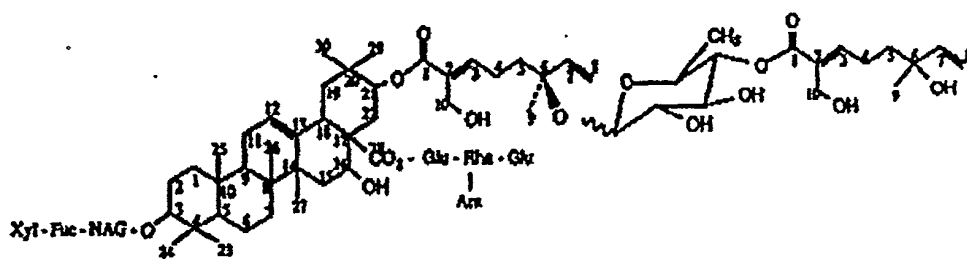
FIG. 55 A, B



IC₅₀ Values

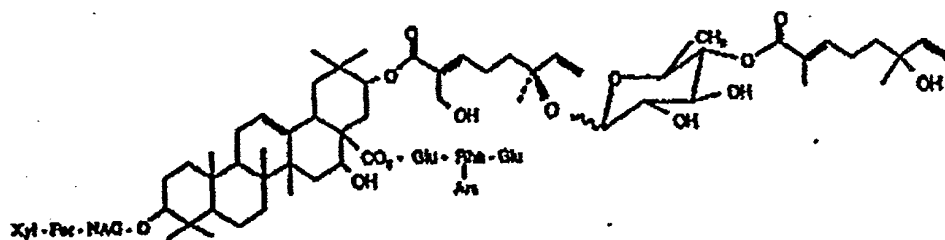
HPLC Separation of the Avicins in F094

0.331-0.407 $\mu\text{g/ml}$



Avicin D

0.320-0.326 $\mu\text{g/ml}$



Avicin G

0.160-0.181 $\mu\text{g/ml}$

FIG. 56

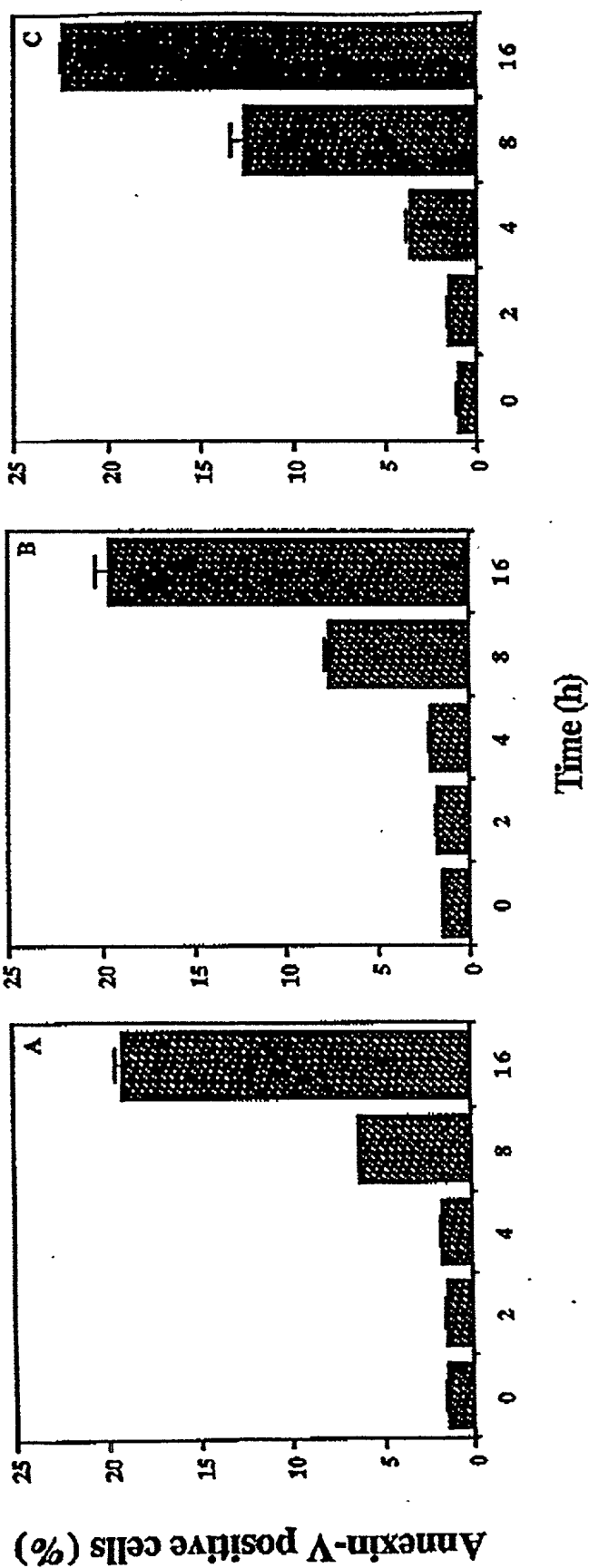


FIG. 57

Time (h) 0 0.5 1 2 4



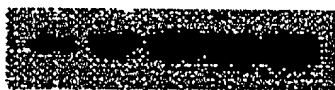
Mixture

Fold increase 1.0 0.8 0.8 1.3 1.5



Avicin D

Fold increase 1.0 1.5 1.7 1.9 3.5



Avicin G

Fold increase 1.0 3.5 4.7 6.3 8.4

FIG. 58

Time (min) 0 1 2 5 10 20

~~mta~~ ~~mta~~ ~~mta~~ ~~mta~~ ~~mta~~ → Cyt-c

Avicin G ($\mu\text{g/ml}$) 0 0.03 0.12 0.5 2 5

 * * * * * * \rightarrow Cyt-c

Untreated
DEVD
zVAD-fmk
Avicln G
DEVD+Avicln G
zVAD-fmk+Avicln G

→ Cyt-c

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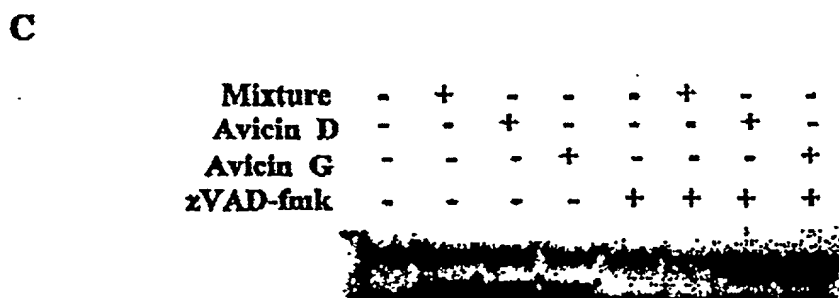
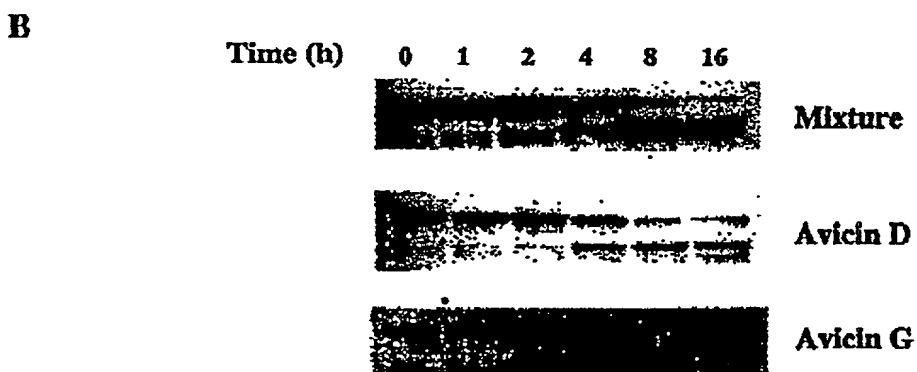
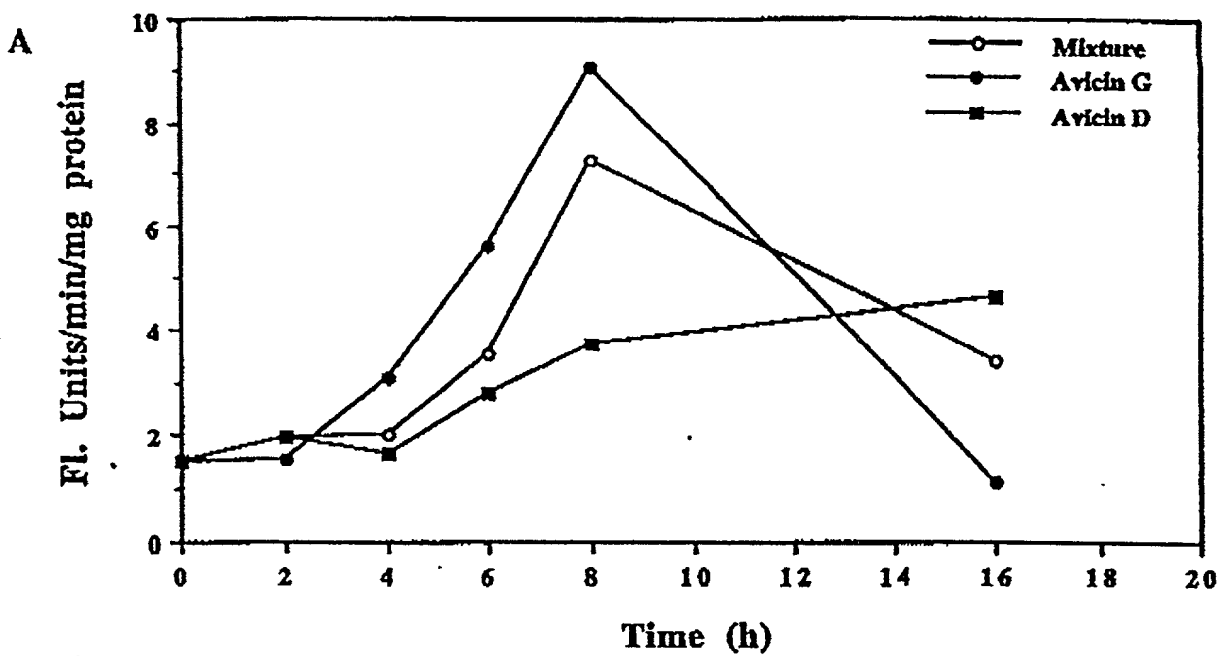


FIG. 60

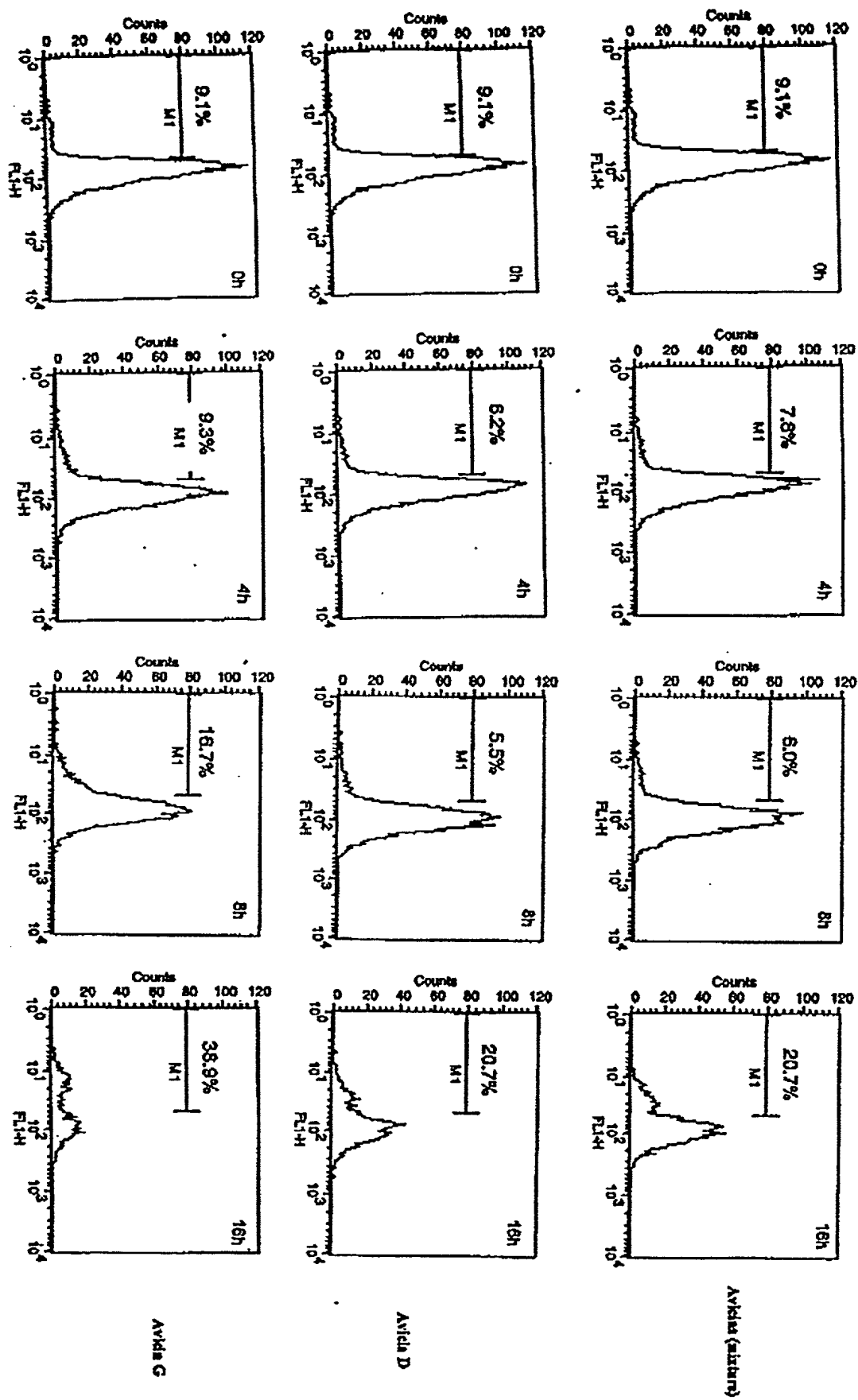


FIG. 61

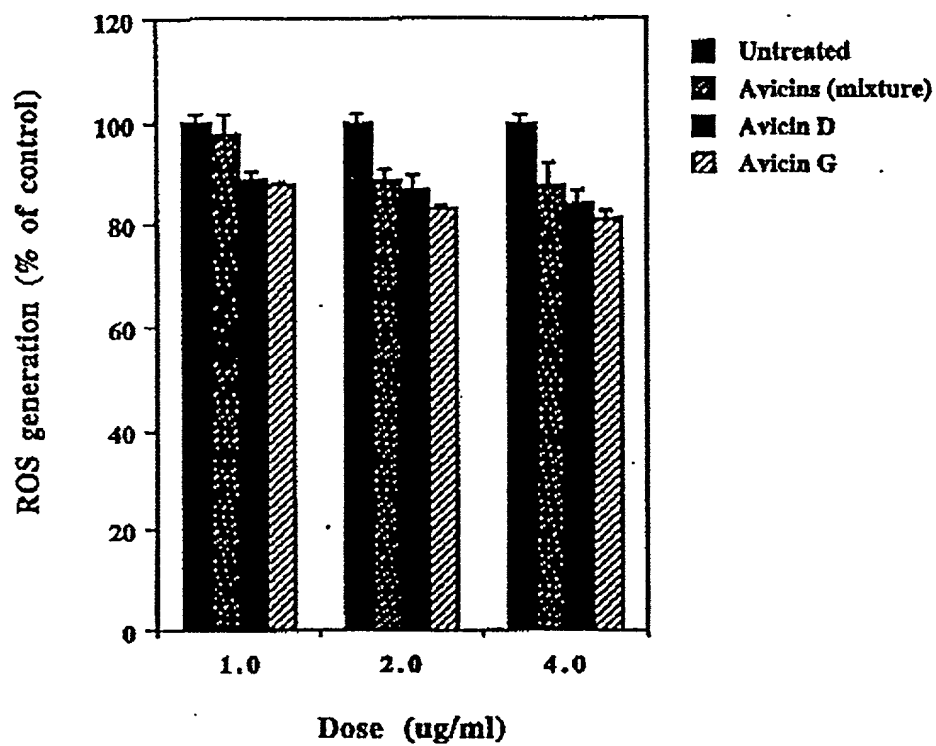


FIG. 62